Harvard Medicine

AUTUMN 2010

Twists of Fate

What can personalized medicine reveal about your future?

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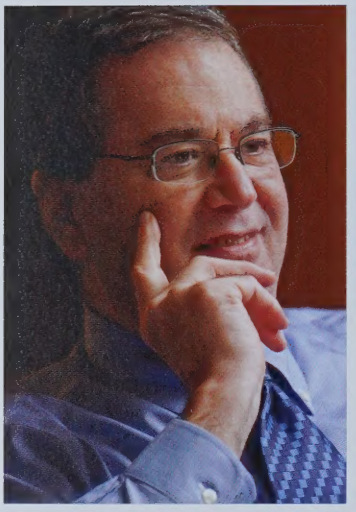
From the Dean

THOUGHTS ON INNOVATION



Within seconds of the baby's birth, a single drop of blood reveals his odds: neurological disease, 60 percent risk; bipolar disorder, 42 percent risk; heart defect, 99 percent risk. He's a de-*gene*-rate, conceived the old-fashioned way—left to genetic chance. His parents plan their next child more wisely, coached by a geneticist who engineers fertilized eggs free of propensity for disease, blemishes, and even moral turpitude.

In the science fiction movie *GATTACA*, titled from the alphabetic quartet of nucleotides that form DNA's double helix, that flawed baby grows up to prove that probability is not certainty and that our genetic makeup does not define us after all. The movie was released in 1997, midway through the Human Genome Project, at a time of heightened hope and hype about our prospects for tackling disease once we had cracked the genetic code.

A decade has now passed since a working draft of the human genome was announced. While the movie's dystopia has not emerged, neither has the glittering promise of easy answers to the problems of disease. Rather than a revolution in medicine, our growing understanding of genetics has led to an evolution in personalized medicine, the goal of which is to deliver the right therapies to the right people in order to maximize success, minimize side effects, and guide individualized care.

Successes in personalized medicine, particularly within oncology, continue to accrue—many, I am proud to say, at Harvard Medical School and its affiliated institutions. Today we have the opportunity to move away from treatment approaches based on organs and symptoms toward ones that incorporate preventive strategies and a deeper understanding of disease mechanisms. The more we learn, the more we realize that we have barely scratched the surface of what personalized medicine may eventually offer.

We also have an opportunity to cut spending. With the dramatic drop in the cost of sequencing a human genome—from $3 billion to just thousands of dollars in ten years—we can imagine a time when everyone's genome will be sequenced as a routine part of medical care in this country. Consider the cost of *not* taking advantage of tailored treatments: In 2008, according to McKinsey & Company, we spent nearly $300 billion on pharmaceuticals—yet many drugs are fully effective in only 50 to 60 percent of those who take them. And adverse reactions drive as much as $135 billion in needless costs each year.

As our ability to interpret genomic data improves, we hope to reduce health care costs, to avoid trial-and-error prescribing, to prevent adverse drug reactions—and to shift our emphasis from treating symptoms to preventing disease. I hope this issue of *Harvard Medicine* shines some light on the challenges inherent in our efforts to personalize medicine and provides insight into advances that may one day transform lives.

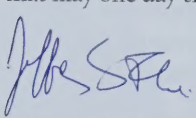


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PHOTO: LEN RUBENSTEIN

Letters to the Editor

SECOND OPINIONS FROM OUR READERS

All in Good Time

Congratulations on the *Harvard Medical Alumni Bulletin*, now *Harvard Medicine!* The publication keeps getting better all the time.

DAVID J. ZALESKE '75
MINNEAPOLIS, MINNESOTA

New Tricks

Dazzling content and a lot of new science. Bravo!

CURTIS PROUT '41
MANCHESTER, MASSACHUSETTS

A Way with Words

I am rarely one to give spontaneous positive feedback, but I was delighted with the new format and content of the magazine. The articles were brief, to the point, and of great interest. I liked the five senses theme. Keep up the great work. Congratulations!

STEPHEN PAUKER '68
WESTON, MASSACHUSETTS

Creative Accounting

Although I am an attorney, not a physician, I avidly read the spring edition of *Harvard Medicine*, which my husband, Edward Landau '54, received. My thanks for your thoughtful innovation and creativity. The issue was fascinating and informative. I not only read but also forwarded several of the enlightening articles to friends and family members. *Harvard Medicine* is eminently readable in its new format and will serve to educate many!

SANDRA S. LANDAU
NORTHBOROUGH, MASSACHUSETTS

Light Reading

I have been a regular, cover-to-cover reader of the *Harvard Medical Alumni Bulletin* for many years because of its interesting content, not necessarily because I wanted to know about every little research project at Harvard Medical School. I read the current issue cover to cover as well. I found the overall appearance of the magazine to be more popular—something to attract a newsstand buyer—than serious. Much of the content was good, in particular the piece by Atul Gawande '94, who is a remarkably talented writer. A lot of other content, though, such as interviews about work in progress, smacked more of *USA Today* than medical journalism. It looks as if you are trying to appeal to a different audience. In so doing, you could lose some of the audience you have had.

RICHARD E. BURNEY '69
ANN ARBOR, MICHIGAN

Dressed for Success

The spring edition is fabulous! I love your new format.

CLAIRE WILSON '77
BURLINGTON, MASSACHUSETTS

Reports Greatly Exaggerated

In "The Sixth Sense" in the spring issue, Allan Hamilton '82 wrote about a case that science could not explain. I found his suggestion of "the glory of God" to be unwarranted. It has been reported that patients under general anesthesia remember statements made in the operating room. Despite the stoppage of her heart and the disappearance of her brainwaves, the patient heard and remembered conversations in the operating room, suggesting that she was not clinically dead. I agree with Hamilton that the mechanism is not evident, but I expect science to have an answer to the mystery eventually.

WARREN GUNTHEROTH '52
SEATTLE, WASHINGTON

The Great Reformation

In your excellent article on a panel discussion on health care reform, two of the panelists, David Goldhill and Daniel Kessler, implied that coverage-driven reform is unlikely to contain costs while maintaining or improving care quality. Hope remains, however. Research at Harvard and elsewhere is providing new insights into the processes of behavior change and medical decision-making. A cross-disciplinary approach that integrates contemporary understanding of brain science, clinical psychology, and public health might provide Harvard Medical School with a leadership pathway to the workable alternatives that Kessler mentioned.

JOHN B. LIVINGSTONE '58
PROVINCETOWN, MASSACHUSETTS

CONFLICTS OF INTEREST

The School's new open-book approach to alliances with industry will soon be just a click away

A third-year Harvard medical student stares at her computer screen, poised to register for courses. She has already taken required classes and research electives. She would like to sign up for gynecologic oncology, but first wants to know whether her instructors have financial ties to the pharmaceutical industry. Within seconds of clicking a link from the HMS homepage, she's reviewing a list of faculty members' financial interests.

This capability does not yet exist—but it soon will, just one of many changes resulting from the School's updated conflicts-of-interest (COI) policy, which goes into effect on a rolling basis beginning in January 2011. Access to an online disclosure resource will soon be the norm for anyone who wants to explore an HMS faculty member's financial ties to industry. The new site, as well as all other aspects of the COI policy, will emphasize transparency, serving to reduce even the appearance of inappropriate industry influence.

The revision of the existing COI policy began in early 2009, when HMS Dean Jeffrey Flier convened a committee of more than 30 faculty and students to critique the HMS Policy on Conflicts of Interest and Commitment. The committee presented its recommendations to Flier in the spring of 2010; by July, he had reviewed and accepted those recommendations.

"At HMS, we have a proud history of unwavering commitment to high professional standards of ethical conduct," Flier says. "Within and outside industry, many recognize that industry and academia must seek a new model of academia–industry collaboration to achieve greater success at discovery and development of new treatments while fully protecting academic values and those of the medical profession. We must create a culture that is open to creative new approaches to collaboration on scientific development, based on transparency, rather than one that makes novel interactions more difficult."

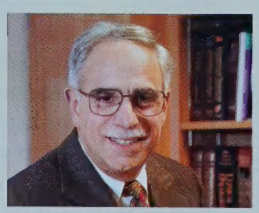
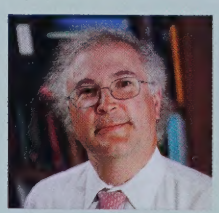
While reaffirming that academia–industry collaborations are key to turning laboratory discoveries into patient therapies, the committee's recommendations emphasized the need to avoid marketing influences from industry.

"HMS faculty are committed to the highest ethical standards in research, patient care, and the education of current and future health care providers," says Robert Mayer '69, the Stephen B. Kay Family Professor of Medicine at Dana-Farber Cancer Institute and chair of the Standing Committee on Conflicts of Interest and Commitment. "We believe that these policy revisions will guide them as they fulfill their commitment."

For more information, visit hms.harvard.edu/public/coi.

Key Guidelines

- **Create** a uniform and accessible reporting system for faculty at Harvard Medical School and its affiliated institutions.
- **Develop** an education and disclosure monitoring system to help faculty understand and adhere to the new policy requirements.
- **Prohibit** faculty from accepting personal gifts, travel, and meals from industry, other than travel and meals provided in the course of allowed activities.
- **Ensure** academic independence in the creation and delivery of continuing medical education course content, limit industry funding for courses so that no one sponsor funds more than half a course, and restrict industry advertising and exhibitions at continuing medical education events.
- **Ensure** that all relevant faculty financial interests are disclosed publicly, on the Harvard Catalyst website.
- **Prohibit** faculty participation in industry speakers' bureaus and faculty acceptance of compensation for any speaking engagement that limits the faculty member's intellectual independence in presenting content.


OPEN-BOOK AUTHORS: The new conflict-of-interest policy took shape with guidance from committee co-chairs, from left, Joseph Loscalzo, Robert Mayer, Thomas Michel, and Christopher T. Walsh.

PHOTOS (CLOCKWISE FROM TOP): JAN REISS; FRANK SITEMAN; STEVE GILBERT (MICHEL AND MAYER); COURTESY OF BRIGHAM AND WOMEN'S HOSPITAL

CHERISH THE THOUGHTS

Harvard uses crowdsourcing to generate ideas on diabetes

Crowdsourcing, the practice of solving problems by tapping the creativity of large groups rather than individual experts, has solved puzzles in fields such as marketing, engineering, and software design. But can the wisdom of crowds help cure disease?

In February, Harvard Catalyst, the HMS clinical and translational research center, asked Harvard's community as well as the general public to answer the question: What do we need to know to cure type 1 diabetes?

"We invited people to share their out-of-the-box questions and proposals," says Lee Nadler '73, Harvard Catalyst director and HMS dean for clinical and translational research. "We wanted participants to apply their insights to this question."

The invitation worked. The competition received 190 entries from which a large, multidisciplinary panel selected a dozen pioneering ones. Winning ideas came from people with diabetes, graduate students, a college student, a human resources representative, and researchers who are not experts in the field.

Among the entries chosen were ones that called for fine-tuning diabetes management by developing a numerical scale for personalizing treatment; investigating immune system interactions with lipids as well as with cells and proteins for insights into the disease; and developing "smart" liposomes that could carry diabetes drugs directly to the pancreas. Working with the Leona M. and Harry B. Helmsley Charitable Trust, Harvard Catalyst plans to solicit proposals from within the Harvard research community to carry out some or all of the winning ideas.

Visit hms.harvard.edu/public/news/2010/092910_innocentive for details about the winners and their ideas.

PHOTOS: STEVE LIPOFSKY (RIGHT); DR. DAVID M. PHILLIPS/VISUALS UNLIMITED/GETTY IMAGES (FAR RIGHT)

EMERGING TALENTS: More than 200 medical and dental students officially kicked off their Harvard professional training in August by donning their ceremonial white coats.

A Boost for Immunology

Harvard immunology experts recently gained a new mechanism through which they can pool their talents when HMS Dean Jeffrey Flier announced the launch of Harvard Immunology, an initiative that aims to inspire collaboration in this field.

"Harvard Immunology will be committed to gaining a better understanding of the normal biology of immune and inflammatory systems, host defense, and altered states of immunity, with the ultimate goal of preventing and treating human illness," Flier says. "We are eager to bring together basic, translational, and clinical investigators to achieve these goals."

Harvard Immunology will connect both longstanding and new entities, including the Committee on Immunology at Harvard—which has long overseen the HMS graduate immunology program—and, within the Department of Microbiology and Immunobiology, a new Division of Immunology, which will nurture and develop a community of immunologists on the HMS campus.

The initiative has also prompted the creation of the Harvard Institute of Translational Immunology, which will convene multidisciplinary basic, translational, and clinical investigators from HMS and its affiliates to study immune-mediated diseases.

"Although Harvard's diverse and accomplished immunology community is world-class by any standard," Flier says, "we believe we can further spur progress."

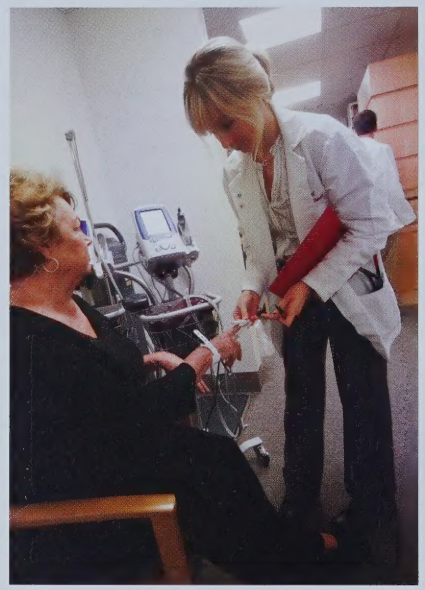
A BRIDGE TO CARE

Medical students help fill the primary-care gap

Medical students eager for clinical experience in primary care have taken proactive learning to a whole new level. The student-designed Crimson Care Collaborative, a practice run by both faculty and students at Massachusetts General Hospital, has a twofold mission: to enrich medical education in primary care and to expand access to primary-care services for both insured and uninsured patients. Students and their preceptors recently opened the doors of the new collaborative.

"The idea that students could be mobilized to address the crisis over the lack of access to primary care is very appealing," says Camille Powe '11, whose ideas helped lay the groundwork last fall. "It was easy to recruit students; we were inundated from the start."

The student–faculty collaborative practice aims to nurture enduring relationships, says David Bayne '11. Every patient sees a physician, but students also follow the patients over time. Patients can access social services as well. "Our strategy is to see patients who don't have doctors, then to link them up with a more permanent primary-care provider," Bayne says. "That's a big part of our mission: providing a bridge to care."



DOCTOR IN TRAINING: Emily Morell, a second-year HMS student, takes the vital signs of a patient attending the Crimson Care Collaborative clinic.

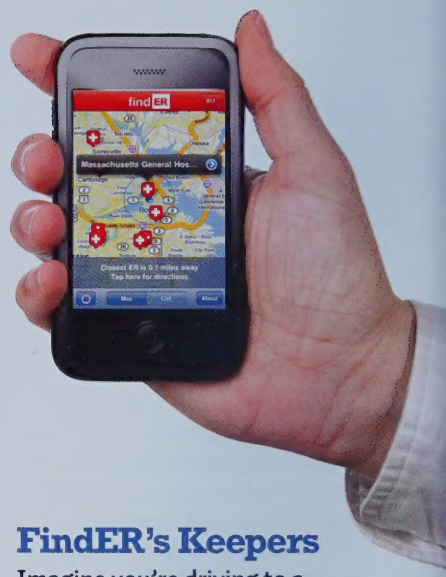
The Crimson Care Collaborative was conceived by Rebecca Berman '05, an HMS instructor in medicine at Mass General and a physician fellow at the hospital's John D. Stoeckle Center for Primary Care Innovation. Enlisted by the center to promote student interest in primary care, Berman reports that candidates for internal medicine residencies who have had experience in student clinics at other schools typically rave about them. HMS has never had a clinic that engaged students in weaving a health care safety net for patients. But given the requirements for health insurance now in effect for Massachusetts residents, Berman says, the influx of newly insured patients has overwhelmed Massachusetts' primary-care providers, and HMS students are eager to address the shortage of practitioners.

Under Berman's guidance, a nucleus of students shaped the clinic's practice model; more than a hundred students have been involved since planning began in the fall of 2009. Patients are seen initially by first- or second-year students who take vital signs; third- and fourth-year students complete medical histories and conduct physical exams. Berman works with the students in developing each patient's treatment plans. "The clinic will cater to urgent-care patients as well as patients who lack a primary-care doctor," Berman says.

Meanwhile, the students have their eyes on the bigger picture. "Primary care can help solve the problems we have with our health care system," Powe says. "If people have good relationships with their primary-care providers, they're less likely to get a lot of unnecessary tests and specialty treatments, and they won't go to emergency departments as often. Better access to primary care is economical, and it's also better for patients' health."

"Our students are designing a model to increase access to primary care across the country," Berman says. "Harvard creates leaders, and we need leaders in primary care."

To learn about innovations in synthetic biology, view the recent "How to Create Life" program >> hms.harvard.edu/community/talksattwelve/#life



FindER's Keepers

Imagine you're driving to a beach hours from home when your son suddenly starts wheezing. Beads of sweat trickle down his forehead. He tries to speak but can only issue raspy coughs. You desperately scan the highway for a blue sign with a reassuring white "H," but no such sign appears.

You quickly tap the findER icon on your iPhone and, within seconds, a map highlighting the nearest emergency departments flashes into view. You hit an icon for a hospital just a few miles away and, following the directions, race your child to medical help.

Researchers at the Massachusetts General Hospital Emergency Medicine Network, or EMNet, recently launched the findER application to help people in just such emergencies.

"FindER accesses information on the nearly 5,000 emergency departments in EMNet's database, which is the most complete and accurate in the nation," says Carlos Camargo, the network's director and an HMS associate professor of medicine at Massachusetts General Hospital.

Along with directions and general information, findER offers on-screen options for users to call hospitals directly and even to reach emergency care personnel. To download the free application from the iTunes app store, search for "EMNet findER."

PHOTOS: JOSHUA TOUSTER (LEFT); MATTIAS PALUDI (ABOVE)

THE DRAMA OF MEDICINE

A television documentary series shines a spotlight on three Harvard hospitals

For first-grader Olivia Quigley, the school day began like any other. But it suddenly became far less ordinary when, in gym class, Olivia collapsed on the basketball court. Within minutes, she was lifted into an ambulance and raced to Massachusetts General Hospital with a diagnosis of sudden cardiac arrest. As her parents hovered anxiously, the emergency staff sprang into action to save the six-year-old.

Mass General surgeons implanted a defibrillator, and Olivia received rehabilitation therapy. Other than suffering minor speech and memory impairments, she has made a remarkable recovery.

Olivia's story and those of dozens of others were recounted on *Boston Med*, a documentary drama that aired this past summer on ABC. The eight-hour series, filmed over four months, followed physicians, nurses, and patients at three Harvard-affiliated hospitals: Brigham and Women's Hospital, Children's Hospital Boston, and Mass General. The series depicts a range of crises, from an infant born with a heart defect to a pregnant woman shot in the chest, a sixteen-year-old awaiting a heart transplant, and a man facing treatment for mesothelioma.

"We spent a great deal of time thinking about and weighing the various risks and benefits of participating in such a long-term, intense project," says Peter Slavin, president of Mass General. "Ultimately, our decision to participate was based on the incredible opportunity to shine a spotlight on the many dimensions of academic medicine."

"*Boston Med* is about some extraordinary places where critical decisions are commonplace, where poignant moments abound, where failures can devastate, and where triumphs are savored," Slavin adds. "The stories that emerge from these places are heartwarming, heart wrenching, and heartening. And they deserve to be told."

Episodes can be viewed online at abc.go.com/watch/bostonmed/SH5570013.

CASTING CALL: Harvard hospital staff recently starred in a documentary series on health care.

PHOTO: DONNA SVENNEICK/ABC NEWS

Bragging Rites

It's been another banner year for Harvard Medical School and its affiliates. According to annual rankings by *U.S. News & World Report*, HMS placed first among U.S. research medical schools for the 21st consecutive year, and its affiliated institutions received high marks as well. In the magazine's honor roll of America's Best Hospitals, Massachusetts General Hospital placed third, while Brigham and Women's Hospital ranked eleventh. Only 152 of 5,000 U.S. medical centers ranked in one or more specialties; of those, just 14 also earned berths on the honor roll.

Mass General was among the top ten hospitals in 14 specialties, with psychiatry again garnering first place. The hospital placed second in diabetes and endocrinology and otolaryngology; third in neurology and neurosurgery and orthopedics; fourth in geriatrics, ophthalmology, and gastroenterology; fifth in heart and heart surgery, pulmonology, kidney disorders, and gynecology; and seventh in rheumatology and oncology.

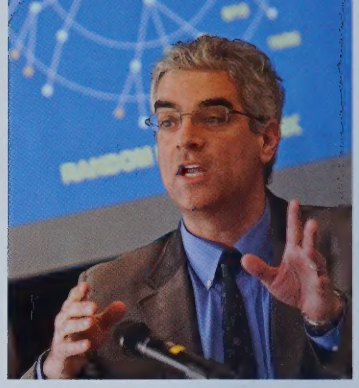
Brigham and Women's placed in the top ten in five categories: gynecology, rheumatology, kidney disease, heart and heart surgery, and diabetes and endocrinology.

Among other HMS affiliates, McLean Hospital placed third in psychiatry; Spaulding Rehabilitation Hospital placed fourth in rehabilitation; Dana–Farber Cancer Institute ranked sixth in cancer; and Massachusetts Eye and Ear Infirmary shared accolades with Mass General for otolaryngology and ophthalmology.

In a separate ranking of pediatric institutions, Children's Hospital Boston placed first in five specialties, more than any other U.S. children's hospital. Its standouts included heart and heart surgery, neurology and neurosurgery, kidney disorders, orthopedics, and urology. Children's was the only hospital to place in the top three for all ten pediatric specialties assessed.

In addition, in its first evaluation of U.S. doctoral programs in 15 years, the National Research Council ranked each of Harvard's four Division of Medical Sciences programs at the top, with all of them ranked first at least once.

"Such results," says Jeffrey Flier, dean of HMS, "validate the unparalleled work of our faculty in their efforts to train future leaders in biomedicine."



MATCHMAKER: Nicholas Christakis looks at how social networks affect people's lives.

THE MATING GAME

Competition in courtship, when fierce, can shorten men's lives

Boys who attend high school with too few girls may suffer the consequences long after prom. Men who reach sexual maturity where they outnumber women live three months less than the average life expectancy among peers whose competition for a mate isn't as fierce, an HMS-led study suggests. The steeper the gender ratio, the shorter the lifespan.

Gender ratios and longevity have been linked in animals. To learn whether a connection exists in humans as well, Nicholas Christakis '88, senior author on the study and an HMS professor of medicine and of medical sociology, collaborated with researchers in the United States and China. Looking at men who graduated from Wisconsin high schools in 1957 and, separately, at a national sample of more than 7 million U.S. men, the researchers saw similar results. Their findings appeared in the August issue of *Demography*.

The social costs of gender imbalances are well documented in China and India, where selective abortion and other factors have led to men outnumbering women by 20 percent in some regions. Such male-dominant environments, already linked to greater violence and human trafficking, may shorten life as well.

Christakis suspects that a combination of social and biological factors may account for this curtailment. Finding a mate can add stress—a known health hazard. "We literally come to embody the social world around us," Christakis says, "and what could be more social than the dynamics of sexual competition?"

Win Friends and Influence Influenza

Your friends are probably more popular than you are. Curiously, this "friendship paradox" may help predict disease outbreaks.

Noted nearly two decades ago, the friendship paradox holds that, statistically, the friends of any given individual are likely to be more popular than she is. Take a random group of people, ask each to name one friend, and on average that friend will rank higher in the social web. And those popular friends will collect gossip, trends, ideas—and, it seems, diseases—sooner than their less connected counterparts.

Monitoring those pivotal members of social networks is an ideal way to predict outbreaks, Nicholas Christakis '88, an HMS professor of medicine and of medical sociology, and James Fowler of the University of California, San Diego, found when they applied the friendship paradox to the 2009 flu epidemic. As influenza season approached, they contacted 319 Harvard undergraduates who, in turn, named 425 Harvard friends. And lo: those friends manifested flu symptoms up to 46 days sooner than the rest of the student population. The study appeared September 15 in *PLoS ONE*.

"Public health officials often track epidemics by following random samples of people or monitoring people after they get sick," says Christakis. "But by simply asking members of the random group to name friends, and then following both groups, we can predict epidemics before they strike the population at large."

PHOTOS: DOMINICK REUTER/HARVARD NEWS OFFICE (ABOVE); PETER GRIFFITH/GETTY IMAGES

Visit Harvard Medical School's Idea Lab, a virtual laboratory for sharing thoughts on biomedicine:

HOME REMEDY

Dying at home benefits terminal patients and their caregivers

For people with terminal cancer, having the option to die at home rather than in the hospital results in higher quality-of-life scores at life's end—and may improve quality of life for caregivers too.

A study published October 10 in the *Journal of Clinical Oncology* found that when people died at home, their loved ones were less likely to develop post-traumatic stress disorder or prolonged grief disorder, a condition marked by intense, disabling grief that lasts longer than six months.

"Where someone dies has important implications for those they leave behind," says lead author Alexi Wright, an HMS instructor in medicine at Dana-Farber Cancer Institute. Wright points out that while most cancer patients would prefer to die at home, that's not always possible. More than one-third die in a hospital, and 8 percent die in intensive care.

Wright believes the frightening nature of aggressive lifesaving care, such as cardiopulmonary resuscitation and mechanical breathing devices, may come at a high cost. "Making the quality of life better for a patient with a terminal diagnosis is often more valuable," she says, "than attempting to extend life at the cost of quality."

Life Before Death

Palliative care not only provides a better quality of life to patients with terminal cancer, but may also help them live two months longer than patients receiving standard care alone, researchers at Massachusetts General Hospital report.

Cancer patients traditionally receive palliative care—help managing the psychological aspects of serious illness as well as symptoms such as pain and nausea—late in their illness. Study participants—all recently diagnosed with metastatic non–small-cell lung cancer—were randomly assigned to receive either standard oncology care or early palliative care in addition to standard care. Even though aggressive end-of-life care was more common in the standard-care group than in the palliative-care one, patients in the latter group lived approximately two months longer than those in the former group and showed improvements in both quality of life and mood.

"One of the most common misconceptions about palliative care is that it means giving up," says Vicki Jackson, an HMS instructor in medicine and a coauthor of the study, which appeared in the August 19 issue of *The New England Journal of Medicine*. "These patients not only lived longer, they also experienced improved quality of life and were better able to enjoy the time they had remaining."

GETTING THE RED OUT

Replacing red meat with nuts, fish, or poultry may save your heart

Replacing just one serving of red meat a day with a packet of nuts could reduce your risk of heart disease by nearly a third. Harvard researchers have found that women who consumed greater amounts of red meat had an increased risk of coronary heart disease, but those who replaced red meat with protein-rich foods such as fish, poultry, or nuts had a much lower risk. Eating one serving a day of nuts in place of red meat was linked to a 30 percent lower risk of coronary heart disease; substituting a serving of fish lessened risk by 24 percent; poultry, by 19 percent; and low-fat dairy, by 13 percent. The findings, which appeared in the August 31 issue of *Circulation*, draw on the long-running Nurses' Health Study, based at Brigham and Women's Hospital.

focushms.com/idealab

PHOTOS: KEN BROWN/ISTOCKPHOTO.COM (RIGHT); KUZMA/ISTOCKPHOTO.COM (FAR RIGHT)

INSIDE INFORMATION

A fresh way to yield adult stem cells without the risks

It's a stop-the-presses kind of discovery. With colleagues, Derrick Rossi, an HMS assistant professor of pathology at the Immune Disease Institute, has devised a new way of producing induced pluripotent stem (iPS) cells. His technique, published in the November 5 issue of *Cell Stem Cell*, has so upended work at the Harvard Stem Cell Institute that researchers there plan to abandon other production techniques and to adopt the new method.

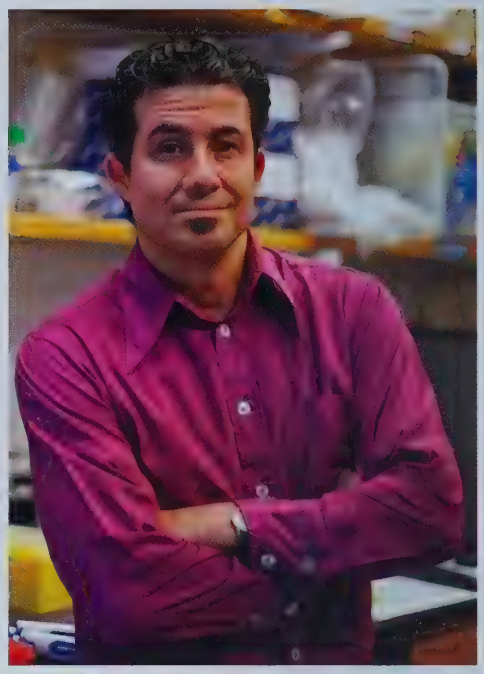
Researchers favor iPS cells not only because the cells can be tailored to a specific patient and a specific disease, but also because they can be derived from adult cells, skirting the need to harvest cells from embryos, a controversial source. But clinical use of iPS cells has been hampered by problems.

First, generating iPS cells has meant using viruses to introduce reprogramming factors into cellular DNA so as to nudge the cells back to a pluripotent state. Viruses, however, can trigger cancers. Rossi's team elected to use messenger RNAs, modified to avoid triggering the cell's normal antiviral response, to add the reprogramming factors. This use of mRNA spawned a new name: RiPS, short for RNA-iPS cells.

Second, previous methods produced extremely low numbers of usable iPS cells. Rossi's method broke that barrier by yielding usable iPS cells in quantities that are orders of magnitude greater than current yields.

Finally, reprogramming iPS cells has involved the manipulation of growth mediums or the addition of constraining factors. Rossi's team instead used their mRNA technology to direct the fate of the iPS cells into muscle cells.

"Although we developed this technology for cellular reprogramming," says Rossi, "its utility extends far beyond that. It offers a way to get a cell to express any protein without triggering the cell's antiviral response pathways."



TRANSFORMERS: Derrick Rossi and colleagues have found a new way to reprogram adult stem cells.

Life by Chocolate

Can chocolate protect the heart? It sounds sweetly suspect, but women who eat chocolate in moderation appear to lower their risk of heart failure, researchers at Beth Israel Deaconess Medical Center recently reported in the journal *Circulation: Heart Failure*.

In a nine-year study of 31,823 middle-aged and elderly Swedish women, those who ate one to two weekly servings of a high-quality chocolate—with more than 50 percent cocoa content, similar to products marketed in the United States as dark chocolate—had a 32-percent lower risk of developing heart failure, a benefit earlier studies have linked to compounds called flavonoids. Yet women who consumed at least one serving daily gained no benefit.

"You can't ignore that chocolate is a calorie-dense food and that regularly consuming large amounts will raise your risk for weight gain," says lead researcher Murray Mittleman, an HMS associate professor of medicine. "But if you're going to have a treat, dark chocolate is probably a good choice, as long as it's in moderation."

Detail to Attention

Cognitive behavioral therapy, together with medication, significantly reduced symptoms in adults with attention-deficit hyperactivity disorder, or ADHD, according to the first full study to assess a nonmedical treatment of the disorder.

Patients receiving the therapy, which teaches life skills to help handle challenges and curtail negative thinking, had a significant easing of ADHD symptoms that they maintained for 12 months. Those who received medication with relaxation techniques and educational support showed no change in symptoms, according to research published August 25 in *JAMA*.

Medications alone may not ease ADHD patients' difficulty with important daily living skills, such as organizing, says study author Steven Safren, an HMS associate professor of psychology at Massachusetts General Hospital.

PHOTOS: JUSTIN IDE/HARVARD NEWS OFFICE (ABOVE); STEPHEN MORRIS/ISTOCKPHOTO.COM

Lost Generation

Teens today don't hear as well as they used to. So say researchers at Brigham and Women's Hospital, who reported that hearing loss in adolescents has increased during the past 15 years.

Hearing loss is a common and under-recognized public health problem that can undermine a child's educational, psychological, and social development. The study, led by Josef Shargorodsky, an HMS clinical fellow in otology and laryngology at the hospital's Channing Laboratory, and published August 18 in *JAMA*, is one of the first to examine the prevalence of hearing loss among young people over time.

Studying recent and 20-year-old health data for people aged 12 to 19, researchers found that one in five contemporary adolescents shows some evidence of hearing loss, while one in 20 has at least mild hearing loss—respective increases of 31 percent and 77 percent.

The researchers cautioned that more study is needed to explain this erosion of hearing, but the popular media has a suspect on their playlist: the iPod's ubiquitous earbuds.

The iPod Inspectors

Most college students using portable music players exceed recommended decibel exposure limits, researchers report in a study scheduled to appear in the February 2011 issue of the *Journal of Speech, Language, and Hearing Research*. A research team that included Brian Fligor, an HMS instructor in otology and laryngology at Children's Hospital Boston, found that more than half of New York City university students surveyed were at risk for noise-induced hearing loss.

Do Not Disturb

Will a whisper wake you? In the August 10 issue of *Current Biology*, researchers at Massachusetts General Hospital linked fluctuations in the brain's electrical field—marked by brief buzzes of activity, called sleep spindles—to an individual's ability to sleep through noise. Jeffrey Ellenbogen, an HMS assistant professor of neurology, believes this finding can set the stage for developing techniques to help hospital patients sleep amid monitors with noisy alarms.

IT'S ALL IN THE TIMING

A matter of weeks can mean the difference between life and death

A new method of treating patients infected with both HIV and tuberculosis could save countless lives in the developing world, where nearly half a million people die every year from this deadly disease combination. The technique does not require expensive new therapies. It's a simple matter of timing.

Researchers working in Cambodia found that when they initiated an HIV regimen—known as highly active antiretroviral therapy—two weeks after beginning tuberculosis treatment, patients' risk of death fell 34 percent compared to the death risk rates among those starting after the standard eight weeks. The researchers presented their report at the 18th International AIDS Conference, held in July in Vienna.

Senior author Anne Goldfeld, HMS professor of medicine at Brigham and Women's Hospital, has described the two infections as a "match made in hell." An estimated 1.37 million people are infected with both diseases, and tuberculosis kills one quarter of all HIV-infected people.

ON THE ROAD: Sok Thim (left) and Anne Goldfield (right), cofounders of the Cambodian Health Committee, conduct an at-home visit with a tuberculosis patient.

PHOTOS: VSTOCK/TETRA IMAGES/GETTY IMAGES (ABOVE); JAMES NACHTWEY

REACH FOR THE SKY: This steel sculpture of a DNA strand provides a focal point for the Centre for Life in Newcastle upon Tyne in northern England. Charles Jencks, the landscape architect who designed the sculpture, often takes his inspiration from genetics, fractals, and chaos theory.

The human genetics field has been delivering

spectacular science. But can it personalize medicine?

Twists of FATE

by Elizabeth Dougherty

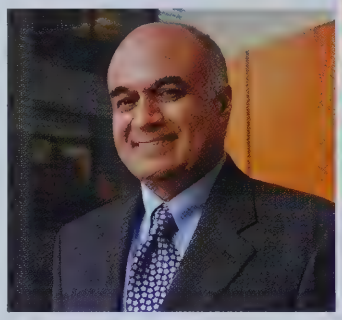
Kate Robbins was in her mid-forties when she began writing a journal for her children. Knowing she had only a few months before her metastatic lung cancer would take her life, she wanted to leave her young son and daughter words of comfort. Those few months of survival have since turned into years, however, and Robbins's journal has been stashed in a closet. The reason? An experimental therapy that unexpectedly melted her tumors. ■ Robbins's unusual response to treatment provided not only joy to her and her family, but also delivered a startling insight to oncologist Daniel Haber. In the fall of 2003, Haber, who directs the Massachusetts General Hospital Cancer Center, was midway through a bowl of Cheerios and the *Boston Globe* when he came across a story about Robbins.

He learned that she was among a small sample of patients whose non–small-cell lung cancer had successfully responded to the drug gefitinib, marketed as Iressa. Her miraculous reprieve could only be explained by genetics, he thought. He immediately called her doctor.

Haber's collaboration with that doctor, Thomas Lynch, then an HMS professor of medicine at Mass General, led to the discovery of a gene-linked wrinkle to the drug's effectiveness. Their research found that Iressa could bind well to a protein known as epidermal growth factor receptor, or EGFR, but that the tightness of this drug–protein bond increased tenfold if the gene that produced the protein had mutated during the development of the tumor, as in Robbins's case. That work—along with simultaneous research by a team of scientists from the Dana-Farber Cancer Institute and Brigham and Women's Hospital, led by Matthew Meyerson '89, an HMS professor of pathology—gave rise to a genomics test that could predict, simply by analyzing lung-tumor tissue DNA, which patients would benefit from the drug.

Today, DNA from lung tumors can be sequenced to determine the genetic mutations that drive a tumor's growth so that targeted, more effective treatments can be selected. Tarceva, a drug with action similar to that of Iressa, has now succeeded Iressa as a first-line treatment for non–small-cell lung cancer; second-line treatments have since been added to the clinical arsenal as well.

TAILOR MADE: Raju Kucherlapati (below) and Mark Boguski (below right) are helping to develop targeted therapies they hope will prove as effective as the one that saved Kate Robbins (right).



Researchers have dubbed this kind of precision diagnosis and treatment *personalized medicine*, an umbrella term for a range of approaches that mine genetic data to bring greater resolution to the often murky factors that contribute to disease—and maybe *(just maybe!)* identify precise, targeted therapies.

Where personalized medicine ends up may well depend on how doctors and scientists define it during this time of rapid discovery and change. And medicine as we know it *is* changing fast. The first sequencing of a human genome cost nearly $3 billion and took more than a decade to complete. Today the expense runs in the thousands, and it can be done in

PERSONALIZED MEDICINE MILESTONES AT HARVARD

A sampling of the many initiatives that are helping to shape a clinical revolution

(For a more complete timeline, visit harvardmedicine.hms.harvard.edu/magazine/autumn2010/timeline.php)

1984

George Church, now an HMS professor of genetics, collaborates with Harvard professor and Nobelist Walter Gilbert to develop the first direct genome sequencing method. Both scientists go on to help initiate the Human Genome Project.

Note: Entries whose years are marked in black relate to the Human Genome Project and are not specific to Harvard.

1990

The Human Genome Project officially launches, with the goals of identifying all human genes and sequencing the 3 billion bases of a composite human genome.

2000

U.S. President Bill Clinton and British Prime Minister Tony Blair jointly announce that scientists with the Human Genome Project have completed a rough draft of the human genome. "Without a doubt," Clinton says, "this is the most important, most wondrous map ever produced by humankind."

PHOTO: JUSTIN KNIGHT; COURTESY OF THE PARTNERS HEALTHCARE CENTER FOR PERSONALIZED GENETIC MEDICINE

a matter of months—and even that cost and that timeframe continue to shrink.

Yet amid such change, people define personalized medicine differently, the focus zooming in and out depending on where along the laboratory-to-clinic spectrum the lens is pointed. Personalized medicine could just as easily be called *medicine*—and the need to link a modifier may spring solely from a wish for something to hang onto during the wild ride.

Some of the confusion about this relatively new field may spring not from the realm of medicine, but from the publicity surrounding companies that will crack your distinctive code for a fee. These direct-to-consumer businesses, such as 23andMe and Navigenics, "offer personalized genotyping without a physician in the loop," says Mark Boguski, an HMS associate professor in the Center for Biomedical Informatics, leaving people pondering what, exactly, their long sequence of letters really means and sometimes wondering whether they might rather not have known.

Moreover, some of the confusion stems from the diverse ways in which DNA influences health. Well known are the DNA variations we inherit from our parents. Some are rare and confer a deterministic influence on the so-called genetic diseases, such as cystic fibrosis. Others involve many different genetic variants that interact with the environment, resulting in such common disorders as diabetes and Crohn's disease. And still other mutations are not inherited but simply arise in otherwise normal cells, leading to cancer. Each of these disease categories involves DNA, but the manifestations and the needed therapeutic approaches differ drastically.

In the right settings, however, genetic testing has proved lifesaving. "In these cases," says Raju Kucherlapati, the Paul C. Cabot Professor of Genetics at HMS, "it's no longer the *promise* of personalized medicine. It's actually happening today."

Hitting the Target

Over the past decade, cancer has provided a heartening arena for personalized medicine's promise, demonstrating the clearest success stories thus far. In fact, the Iressa finding was not the first time researchers demonstrated that therapies could target DNA defects arising in tumors.

Several years earlier, for example, the drug Herceptin had been developed based on understanding derived from cancer gene mutations. Herceptin targets breast cancers that over-express the *HER2* gene, which appears in about 30 percent of those with breast cancer. This drug increases survival rates for those testing positive for *HER2* by 33 percent. Another drug, Gleevec, inhibits a malfunctioning enzyme that, based on genetic studies, was discovered to play a role in chronic myeloid leukemia—a diagnosis that essentially amounted to a death sentence before the drug began to extend lives, sometimes dramatically. Gleevec has since been approved for gastrointestinal stromal cancers as well.

Similarly, the Iressa finding represented the first tailored therapy for lung cancers that were otherwise fatal. "Iressa has proven effective in a small fraction of patients," says Kucherlapati, "but for that fraction, the impact has been dramatic." The value of such drugs, Kucherlapati adds, is not just that they can be targeted to the right patients—it's that they target a mutation that is limited to the tumor. Because the mutation doesn't occur in normal cells, the drug has fewer side effects than traditional chemotherapy.

As the field continues to mature, Mass General's Haber predicts, therapies will be targeted at underlying gene abnormalities, regardless of the tissue from which the cancer originated. "You can no longer do cutting-edge oncology without genetic tests," Haber says. "We're finally able to bring to the clinic decades of breakthroughs in understanding the implications of our genes. With advances in both genetics and chemistry, we can now finally see these advances coming together with a very real impact for patients. It's the beginning of a true revolution in the way we treat cancer."

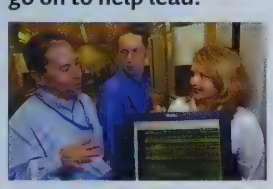
Needles in Haystacks

Slices of the truth of Haber's assessment are evident today. "New information is coming at

PHOTOS: CARLOS DOMINGUEZ (PRECEDING SPREAD); CLOCKWISE FROM FAR LEFT: COURTESY OF RAJU KUCHERLAPATI; SUZANNE KREITER/*BOSTON GLOBE*/LANDOV; PAT GREENHOUSE/*BOSTON GLOBE*/LANDOV

2001

Harvard geneticist Mark Daly observes that DNA recombines in large blocks, or haplotypes. This discovery helps set the stage for the International HapMap Project, which Harvard geneticist David Altshuler '90 will go on to help lead.



2001

The collaboration now known as the Partners HealthCare Center for Personalized Genetic Medicine begins. Within a year, under the scientific direction of Raju Kucherlapati, the center opens a genotyping service to provide precise genomic analyses, especially those of variations known as single-nucleotide polymorphisms, or SNPs, which can signal heightened risk for a given disease.

2003

The Human Genome Project is completed two years ahead of schedule, at a total cost of nearly $3 billion. This milestone coincides with the 50th anniversary of the discovery of the double helical structure of DNA. Harvard's George Church later likens access to data from the project to being able to glimpse the picture on the box of a giant jigsaw puzzle.

2004

Researchers from Massachusetts General Hospital and a team from the Dana–Farber Cancer Institute and Brigham and Women's Hospital independently report that the drug gefitinib—sold as Iressa—produces dramatic benefits in about 10 percent of patients with non–small-cell lung cancer who carry an unusual mutation of a key protein. This discovery offers hope to tens of thousands of patients.

2004

The Broad Institute of MIT and Harvard launches under the direction of Eric Lander, a driving force behind the Human Genome Project. The institute will go on to house one of the largest genome sequencing centers in the world.

PHOTOS, FROM LEFT: JON CHASE/HARVARD NEWS OFFICE; LEN RUBENSTEIN

DAVID ALTSHULER

"I'm skeptical about the promise of personalized medicine when it comes to common and complex diseases."

us fast and furiously," says Kucherlapati, and scientists and technicians are scrambling to validate it and put it into practice. Today, for example, Mass General's cancer center offers molecular fingerprinting—DNA analysis that reveals specific cancer-causing mutations in an individual's tumor cells—for 130 mutations.

Even though few of these fingerprints have corresponding "smart drugs" yet, molecular fingerprints are changing the way doctors diagnose and treat cancer. In fact, the *HER2* mutation, Herceptin's target, has been identified in some types of lung cancer.

Finding such lowest-common denominators of cancer will take time, and a project now under way, The Cancer Genome Atlas, aims to systematize that process. A consortium of researchers—including Harvard affiliates Matthew Meyerson, Lynda Chin, Raju Kucherlapati, and Stacey Gabriel—is sequencing DNA from samples of more than 20 kinds of cancer to look for critical genetic abnormalities. As the atlas expands, Chin, an HMS dermatology professor at the Dana-Farber Cancer Institute and the Broad Institute of Harvard and MIT, expects it to drive development of new biomarkers, new ways of categorizing cancer, and new treatments.

"This project has already changed the way we look at cancer genetics," says Chin. "It's the first step toward a future of personalized medicine, when we no longer lump cancers together by a particular organ site, but treat each as a genetically distinct disease."

The Heart of the Matter

While personalized medicine will no doubt continue to chip away at a number of mutations that arise in cancer cells, there are many other conditions for which genetic testing is used to evaluate the inherited risk of disease. These rare conditions—including Huntington's disease, *BRCA1*- and *BRCA2*-mutated breast cancers, cystic fibrosis, muscular dystrophy, and hypertrophic cardiomyopathy—tend to be caused by a single, inherited genetic component—one mutation in one gene resulting in one disease.

In hypertrophic cardiomyopathy, for example, a genetic defect causes an abnormal thickening of the walls of the heart. This problem can lead to pumping problems and can cause heart failure or sudden death, accounting for the drama of young athletes collapsing unexpectedly on playing fields. In a series of studies spanning the past two decades, HMS professors Christine Seidman and Jonathan Seidman have identified genetic roots for this disorder. Today, Harvard's Laboratory for Molecular Medicine, for which the Seidmans serve as advisors, offers tests for 11 genetic mutations associated with the disorder. Treatment options include the lifesaving implantation of a cardioverter-defibrillator, a device similar to a pacemaker.

Since this heart disorder is inherited, genetic testing is recommended not only for people with symptoms of the disease, but also for the parents, siblings, and children

PHOTOS: LEN RUBENSTEIN (LEFT); JOSHUA TOUSTER, COURTESY OF THEAGEOFPERSONALIZEDMEDICINE.ORG, AND GRAHAM RAMSAY (CLOCKWISE FROM TOP RIGHT); JON CHASE/HARVARD NEWS OFFICE, LEN RUBENSTEIN, AND COURTESY OF THE PERSONAL GENOME PROJECT (BELOW, FROM LEFT)

2005

Researchers from institutions worldwide—including several HMS affiliates—join The Cancer Genome Atlas, a project aimed at characterizing all genomic changes involved in human cancers. The initial goal of mapping three cancers will expand four years later to encompass more than 20 cancers, which, combined, affect at least 10 million people in the United States alone.

2006

George Church receives approval to enroll an initial group of ten volunteers in the Personal Genome Project, an initiative that aims to publish the complete genomes and medical records of all who participate. The web-accessible data of an eventual 100,000 volunteers will allow researchers worldwide to test hypotheses about the relationships between genotype, phenotype, and environmental factors.

2006

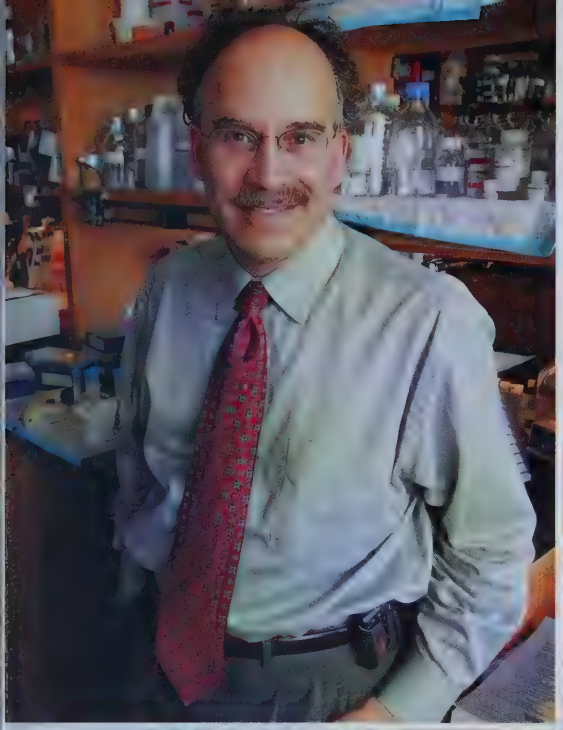
Ting Wu, an HMS professor of genetics, and collaborators in her laboratory initiate the Personal Genetics Education Project to educate a range of audiences, from high school students to physicians, about the ethical, legal, and social issues that will arise in the era of personalized medicine.

2006

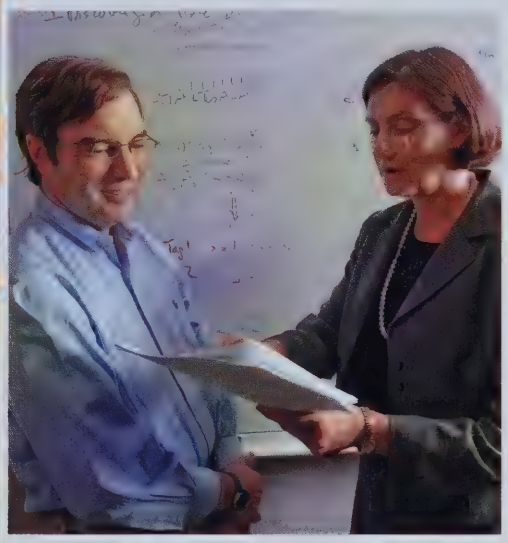
Researchers at Brigham and Women's Hospital and elsewhere create a genetic diversity map that focuses on structural variations known as copy number variants. If the human genome represents the book of life, says principal investigator Charles Lee, this map shows that "sentences can be duplicated or completely deleted in some individuals—sometimes paragraphs, sometimes whole chapters."

2007

By the conclusion of the second phase of the HapMap Project, Harvard contributions include new genetic clues to such conditions as type 2 diabetes, rheumatoid arthritis, and multiple sclerosis.



of anyone diagnosed with it. In one case, Heidi Rehm, an HMS associate professor of pathology at Brigham and Women's Hospital and the Laboratory of Molecular Medicine, found that a young patient carried a harmful cardiomyopathy gene. When she discovered that the patient's father had the same mutation, she asked that all his children be tested as well.



BETTER BY DESIGN: Harvard pioneers in personalized medicine include, clockwise from top, Daniel Haber, Jonathan Seidman, Christine Seidman, Lynda Chin, and Matthew Meyerson.

The undertaking was greater than anyone could have imagined. This particular father had been a sperm donor, and he had 22 biological offspring in addition to the two children he and his wife were raising. "We said, 'Oh my God, this is unbelievable! We have to test all of them,'" says Kucherlapati. Of the offspring the researchers tracked down, nine had the mutation. One had died of heart failure as a toddler, and two were showing symptoms of the disease in their teens. One of those teens has since received a cardioverter-defibrillator.

Kucherlapati believes this case illustrates not just the complexity and power of predictive genomics, but also the uniqueness of each patient. Different mutations call for different interventions. "In one subset of patients, you can implant devices to prevent sudden death," says Kucherlapati, "while another subset has an enzyme deficiency that you can treat with drugs."

Beyond the Magic Bullet

Despite the growing number of success stories in treating certain cancers and in predicting rare genetic conditions, personalized medicine remains a work in progress for many of the most familiar diseases.

"I'm skeptical about the promise of personalized medicine when it comes to common and complex diseases," says David Altshuler '90, HMS professor of genetics and medicine at Mass General and the Broad Institute. "In fact, many diseases are common

2007

The Partners HealthCare Center for Personalized Genetic Medicine creates a test that pinpoints genetic mutations associated with hypertrophic cardiomyopathy, a disorder that can lead to sudden cardiac death. "Personalized medicine," says Christine Seidman, an HMS professor at Brigham and Women's Hospital, "means that we can diagnose disease *and* identify the best treatment approach."

2007

An international team led by researchers at the Dana–Farber Cancer Institute and the Broad Institute produces a comprehensive map of the molecular landscape of lung cancer.

2008

Researchers at the Laboratory for Personalized Medicine at the HMS Center for Biomedical Informatics use cloud computing and clinical avatars for nearly 100 million virtual patients to test dosing of such drugs as the anticoagulant warfarin. "We want to learn," says Peter Tonellato, founder and director of the laboratory, "how to ensure better patient care and better results."

2008

A multi-institutional team announces the results of the largest genomic study to date of lung adenocarcinoma, the most common form of lung cancer. "This work helps identify new targets that might show promise for treating broader groups of lung cancer patients," says co-senior author Matthew Meyerson '89, now an HMS professor of pathology at Dana–Farber Cancer Institute.

2008

The ten pioneers of the Personal Genome Project—including George Church and HMS chief information officer John Halamka—post their genomic data and personal details, from vital signs to biopsy results, on the Internet.

because they have so many triggers, whether genetic, environmental, or lifestyle factors. No single gene explains diabetes, for example. Instead, scientists have identified dozens of genes associated with the disease. No amount of DNA sequencing will turn these complex conditions into single-gene disorders like Huntington's disease."

Even as scientists pinpoint the genetic risk factors for diabetes, Altshuler adds, it isn't likely that testing results alone would change their treatment recommendations. Regardless of degree of risk, the best bet is to maintain a healthy weight and to eat well. In this instance, Altshuler argues, the clinical value of knowing genetic risk factors is debatable.

For Altshuler, the real value of human genetic analysis lies not in diagnostic testing, but in understanding disease. "What limits our progress in many diseases is that we don't know their biological causes," he says. "We need to figure out those causes, then devise interventions that will work for many people because they target the origins of disease."

Along the way, Altshuler believes, some genetic tests will turn out to guide precision diagnoses and treatments, and they should be employed in the clinic as they are proven effective. Yet he points out a potential snag. "If people end up conflating the hype around personalized medicine with the science of understanding disease and developing better interventions," he says, "the entire enterprise could lose credibility."

Getting Personal

Although Sir Francis Galton, a nineteenth-century scientist and proto-geneticist, was eclipsed by his more glamorous half-cousin, Charles Darwin, his legacy is notable nonetheless. A forerunner to the biometrics movement and the inventor of regression analysis, Galton studied height variations in populations, correlating parents and children. While the followers of Mendelian genetics insisted that one gene carried one trait, Galton's adherents saw more of a bell-shaped distribution. The two camps battled it out until Ronald Fisher, widely credited as the founder of modern statistical science, pointed out that the answer was a bit of both: a Reese's Peanut Butter Cup rather than a collision of peanut butter and chocolate. While we inherit genes following Mendel's laws, manifesting a particular trait is hardly a binary equation. A six-foot father and a five-foot mother don't produce children with the exact height of either. Rather, the heights of their offspring range between the two endpoints, even though each child has inherited either the "tall" or the "short" gene.

In many respects, the Mendel–Galton debate continues today between those who hunt for single genes to unlock medicine's mysteries and those who claim that the answer lies in the messy intersection of genes, lifestyle, and environment—those external influences ranging from toxins to traffic-induced stress. Adherents to the latter approach focus on such initiatives as the International HapMap Project and the more recent 1000 Genomes Project. These projects—spearheaded by HMS researchers, including Altshuler and Mark Daly, an associate professor of medicine at Mass General—aim to register every common genetic variant that is likely to appear in a given population.

"The sheer value of all of this for understanding how DNA variation contributes to disease is mind boggling," says Altshuler. "And that's where the true power in genetics lies—not in predicting, but in understanding." Altshuler believes that clues to the most common diseases will be traced only partly to patterns of genetic variants. Their explanation will never be simple, he says, given the confounding influences of environment and scientists' ongoing discoveries about how genes orchestrate life.

An Uncertain Future

As data rush in from ever-larger population studies, advances tailored to individuals are struggling to catch up. By 2015, predicts Boguski of the HMS Center for Biomedical Informatics, doctors will be able to sequence and analyze an individual genome for about the cost of a routine imaging study today. And by 2020, he believes, doctors will be able to analyze a patient's genome during a 15-minute office visit.

"I see a genotype as conceptually no different from a urinalysis or a blood count," Boguski says. "It's just another piece of laboratory

PHOTOS: EVAN KAFKA (RIGHT); CHANNING JOHNSON/*THE WALL STREET JOURNAL* (BELOW LEFT); JON CHASE/HARVARD NEWS OFFICE

2008

The Thrombolysis in Myocardial Infarction (TIMI) study group, based at Brigham and Women's Hospital and led by chair Eugene Braunwald and now vice chair Marc Sabatine '94, announces findings that one-third of people carry a genetic variation that prevents them from properly metabolizing clopidogrel, or Plavix, an antiplatelet medication commonly prescribed to prevent heart attacks.

2009

Massachusetts General Hospital becomes the nation's first to make molecular fingerprinting standard practice in cancer treatment. This bold step helps avoid what Leif Ellisen, an HMS associate professor of medicine, calls "barely educated guesswork" in tailoring treatments to individual patients. "We needed a new way to think about cancer diagnosis and therapy," Ellisen explains.

2009

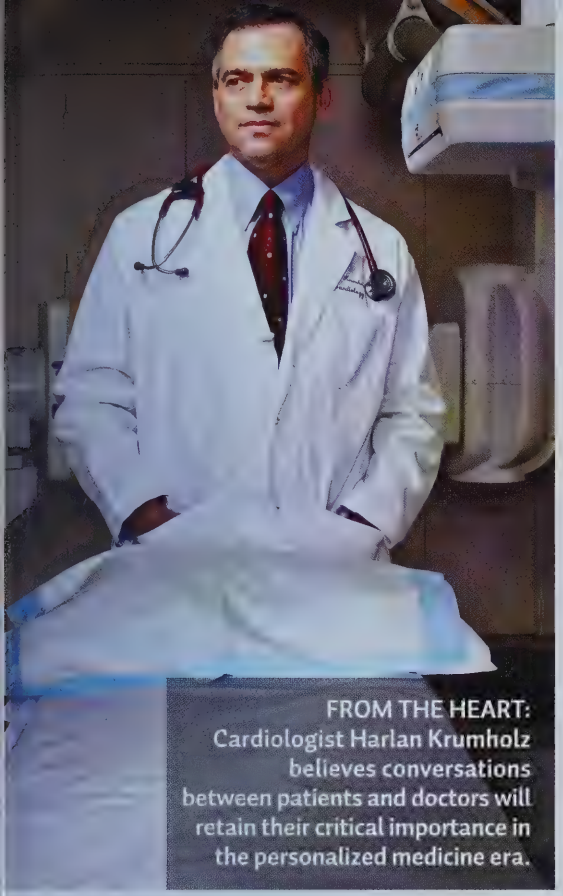
The Department of Pathology at Beth Israel Deaconess Medical Center establishes the country's first mandatory residency training in personalized genomic medicine. A key aspect of the training: residents analyze their own genotype–phenotype associations. "We wanted to figure out strategies," says associate professor Mark Boguski, "for playing a constructive role in this new era of personalized medicine."

2009

Children's Hospital Boston announces the Gene Partnership Project, which allows patients to share a DNA sample and receive, with anonymity, the results of any relevant studies.

2010

Dana–Farber Cancer Institute researchers discover a gene-activity signature that predicts a high risk of cancer recurrence in women with certain breast tumors that have been treated with common chemotherapies. Testing for this signature, say HMS assistant professors Andrea Richardson and Zhigang Wang, could help the 20 percent of women whose cancer recurs because of that gene activity.



FROM THE HEART: Cardiologist Harlan Krumholz believes conversations between patients and doctors will retain their critical importance in the personalized medicine era.

data. In most cases, it's relatively meaningless in isolation, but when we combine it with everything else we know about that patient—medical history, current condition, other laboratory data—that's when we can make sense of it."

Cardiologist Harlan Krumholz '85 agrees. "With the advent of more genetic tests, we may be tempted to think we don't even need to talk to patients anymore," says Krumholz, the Harold H. Hines Jr. Professor of Medicine at the Yale School of Medicine. "We may think we don't need a history. Just give me a set of symptoms and a bar code and I can say from a million miles away what a patient needs. But you can *never* do that in medicine."

Instead, Krumholz envisions working with the patient to chart a treatment course that is in tune with the patient's distinctive biology, medical history, and psychology; only patients, after all, can make the required lifestyle adjustments. But given environmental and other factors that cannot be controlled, Krumholz says, "I'm still going to be left walking my patient through a decision fraught with uncertainty. The precision of a genetic test may help me refine the information or be more confident about my recommendations, but uncertainty will remain. And that uncertainty, I believe, is where real personalized medicine emerges."

The biggest challenge, according to Boguski, will be integrating all the information. "Will primary practitioners need to become geneticists to interpret this? The answer is no," he says. "In the future, doctors will simply deliver genomic findings to patients as part of the larger diagnostic picture." That is, software-based information systems will reduce the 3 billion bytes of genomic information into several bytes a doctor can use to guide clinical decisions. "The challenge for specialists will be to build an infrastructure for those tools," Boguski adds. "For frontline doctors, it's just another medical test. They'll learn how to contextualize it and interpret it in light of everything else they know about the patient."

For all this to happen, Boguski envisions new approaches. He can imagine collaborations, for example, among clinical pathologists, genetic counselors, and molecular medicine experts, and even the emergence of new specialties, such as genetic psychiatry.

More and more patients will likely, out of sheer curiosity, opt to have their genomes sequenced by direct-to-consumer outfits, outside the realm of the clinic, without the support of clinically relevant tools. While many clinicians are wary of potential consequences, Boguski sees the direct-to-consumer opportunity as a "phenomenon of participatory medicine, where patients, or consumers, begin to take increasing responsibility for their health and wellness."

The challenge will also lie in figuring out how to do it now. "Big changes, societal changes, are coming right away," says Kucherlapati. Both CVS Pharmacy and Medco, a prescription-drug benefit provider, for example, will soon start offering genetic tests to patients based on relevance to the prescriptions their physicians write for them. And tens of millions of people will soon be offered genetic tests for clinical reasons, not just for entertainment. And that, says Kucherlapati, "is a lot of people."

Elizabeth Dougherty, a science writer formerly on staff at HMS, is now a freelance writer and novelist living in central Massachusetts.

2010

An international research team announces the discovery of more than 100 genomic sites in which DNA from tumors is either missing or abnormally duplicated. The study shows, says senior author Matthew Meyerson, at the Dana–Farber Cancer Institute, that most of these abnormalities—known as somatic copy-number alterations—are shared across cancers.

2010

Brigham and Women's Hospital embarks on OurGenes, OurHealth, OurCommunity, a study of the effects of genetics, diet, and environment on health. The study will enroll 100,000 patients to enable tailored therapy.

2010

A targeted drug used to treat metastatic melanoma with a specific genetic signature proves successful in more than 80 percent of patients enrolled in a trial. "Metastatic melanoma has a devastating prognosis," says lead author Keith Flaherty, an HMS lecturer on medicine at Massachusetts General Hospital. "These findings can change the outlook for patients whose tumors are fueled by this mutation."

2010

The Broad's David Altshuler, co-chair of the 1000 Genomes Project, coauthors two papers detailing initial findings from the project, which plumbs data from the third phase of the HapMap Project. "Between these two types of genetic variants, very rare and fairly common," Altshuler says, "we have a significant gap in our knowledge." The 1000 Genomes Project aims to fill that gap.

2010

Dana–Farber Cancer Institute researchers uncover a genetic clue that enables doctors to predict, for the first time, the likelihood that children with an aggressive form of leukemia—T-cell acute lymphoblastic leukemia—will benefit from standard chemotherapy. "This will help us determine," says Alejandro Gutierrez, an HMS instructor in pediatrics, "which patients need different regimens."

SPECIAL DECODER KING: George Church has been dubbed "the Edison of genomic sequencing" for his groundbreaking discoveries.

The Personal Genome Project aims to prevent and cure disease with a little help from 100,000 volunteers

by Jessica Cerretani

One is narcoleptic, has high cholesterol, and takes vitamin C. Another struggles with depression and anxiety, is allergic to cats, and wears bifocals. A third has flat feet, type O-positive blood, and the ghost of a scar from a basal cell carcinoma removed a decade ago.

Such details may seem like stray jottings from patients' medical records, or perhaps snippets from dinner-party patter on age-related woes. In fact, they're data from the PGP-10—a group of ten volunteers who agreed in 2006 to have their personal medical information made public as part of the Personal Genome Project. The brainchild of George Church—he of the narcolepsy and vitamin supplements—the project aims to sequence the genomes of 100,000 people. By making the very personal very public, Church hopes that researchers will plumb the information to "develop preventive approaches and cures for disease."

Custom G

TODAY, we can sequence one person's genome for just $1,500. Someday, it may be so inexpensive that people could have their sequencing covered by insurance companies."

The foundation for the PGP was laid in 1964, when researchers at Cornell University and the U.S. Department of Agriculture sequenced the first gene by determining the order of the four bases, or nucleotides, that make up our DNA: adenine, thymine, cytosine, and guanine. Nucleotide chains form the basic recipe for every human.

That discovery had a lasting impact on the nine-year-old Church, now a professor of genetics at Harvard Medical School. A decade later, he was at a computer—rare in biology circles at the time—entertaining himself in a way that perhaps only a budding scientist might. "One day I started typing in all the known DNA and RNA sequences," Church says, describing the numerous combinations of bases. "I thought folding them up was really cool."

Soon, an idea blossomed. "I wondered whether we could sequence *all* the genes in *all* people," says Church. It was, admittedly, a vague and overwhelming plan—but one he thought worth pursuing. Church switched from x-ray crystallography to genetics and began his quest in earnest. By the early 1980s, he and Harvard colleague Walter Gilbert—whose pioneering methods for sequencing the nucleotides in DNA had already earned him a Nobel Prize—had published a strategy for isolating sequences from mouse DNA. That paper, "Genomic Sequencing," caught the eye of administrators at the U.S. Department of Energy, who requested a meeting with Church, Gilbert, and other researchers.

From that 1984 meeting, the concept for the Human Genome Project was born. "We proposed sequencing a complete human genome," says Church. Through a process that married computer technology with laboratory science—namely electrophoresis, which separates molecules like DNA using chemical solutions and a charged electric field—the researchers would map the 3 billion base pairs of the genome. "The Department of Energy leaders acted immediately," Church says. "They didn't ask Congress; they didn't ask anybody's permission. They just started writing checks."

GAME FACE: Technology investor Esther Dyson relishes adventure, whether by training to be a cosmonaut or having her genome sequenced.

PHOTOS: BÉATRICE DE GÉA/*THE NEW YORK TIMES* (PRECEDING SPREAD); STEPHEN BOXALL (THIS PAGE)

To many, it seemed an audacious goal. With so much to sequence, critics charged that the project was impossible to achieve and the cost prohibitive. Yet by 2003, researchers—now funded by the National Institutes of Health—had sequenced the majority of the human genome. The price tag? Roughly $3 billion, or about a dollar a gene.

Sequencing the human genome is one feat. Interpreting it, however, is quite another. The media attention surrounding the project's recent tenth anniversary included commentary from detractors as well as proponents. While biologists continue to be impressed with the project's findings, others point out that the Human Genome Project has yet to deliver on its ultimate promise: to identify the causes of—and propel treatments for—major diseases such as cancer and Alzheimer's. But perhaps such criticism is misplaced. In a recent interview with *Science Watch*, HMS geneticist David Altshuler '90 argues that the project's primary goal "is not to predict disease, nor to personalize medicine. It's to understand the biological systems that underlie common diseases....We're still in the early days."

Church contends that the Human Genome Project has had a huge impact on prediction, enabling the development of up to 2,000 genetic tests. "Some genome centers focused too much on the old methods and on common variants," he says of the project's goals. "If we had prioritized technological advances earlier, then we would have seen an even greater impact." In fact, those advances—significantly expanded since 1984—are what allowed Church to initiate the Personal Genome Project.

Insider Information

By 2003, anticipation began to build around another concept: Could everyone someday

have his or her own genome sequenced? With an estimated cost of $100 million per person, the prospect was clearly out of reach. Yet by 2006, technologies that Church dubs next-generation sequencing—which virtually eliminated the need for electrophoresis—had slashed costs. "Today," he says, "we can sequence one person's genome for just $1,500. Someday, it may be so inexpensive that people could have their sequencing covered by third parties, such as insurance companies."

With affordable technologies in hand, Church and his colleagues were ready to begin the PGP in earnest. But with whose genomes? Like any study, the PGP needed volunteers. The project's scientific and social implications—essentially exposing intensely private information for all to see—led the HMS review board on human subjects to request that the PGP's first group of volunteers be well versed in genomics to ensure that their consent was truly informed.

The first volunteer was one the review board suggested: Church himself. The list of other pioneering participants reads like a *Who's Who* of the scientific and technology worlds. Volunteers include John Halamka, chief information officer of HMS; Harvard psychology professor Steven Pinker; and Esther Dyson, an investor in information technologies.

For Dyson, the decision to participate in the study came naturally. With a mathematician mother, physicist father, and science-historian brother, an appreciation for discovery runs in her family. "I'm reasonably healthy and wasn't concerned about keeping my data private," she explains. "To me, the genome itself is less interesting than what we do with it."

Open Access

It is, in fact, how the PGP data will be used that has scientists alternating between enthusiasm and concern. The open nature of the project—volunteers must be willing to lay bare even the tiniest details of their medical data—has lost some of its shock value in today's Facebook- and Twitter-obsessed culture. Many of us already share our quotidian crises, romantic adventures, personal snapshots, and stray musings on the Internet. It may not be such a leap to make our health information available, too. "The PGP data are useful scientifically," Dyson says. "Why keep them private?"

The benefits of this tell-all approach are clear to Church. "We're trying to determine how different genes, diseases, and environments interact," he says. "That's one reason we want a large pool of volunteers and why we want to make both genomic and trait information available to everyone. If we try to control who has access to that data, then we limit who can make breakthroughs using it." A researcher studying liver health using the PGP data might, for example, make a major advance in the treatment of cirrhosis. But, says Church, that breakthrough just might be made by "the last person you would think to entrust with that data"—a computer programmer, perhaps, or another nonscientist. When it comes to discovery, such open access helps level the playing field.

Church cites this same philosophy when asked about his involvement with companies currently involved in genomic sequencing. He advises more than a dozen such ventures, in the hope that one—or a combination—will improve sequencing technology and drive costs down even further. "It's pretty much like a race to the bottom," he says. "Not that I like races so much, but it's much healthier and more beneficial in the long run to have competition."

Full exposure makes sense from a scientific—and capitalistic—standpoint, but how does it affect participants? Church and his colleagues make every effort to ensure that volunteers understand the full scope of their involvement. To qualify for the study, they must score 100 percent on a test that walks them through the consent process. The test makes clear that volunteering means giving up any control over who views their medical data, which can include conventional electronic medical records and imaging tests like MRI scans, as well as RNA, metabolic analyses, and other information drawn from blood, saliva, and skin samples.

"We don't want to exclude people," Church explains, "but we do want them to know what they're getting into. They have to understand that anyone can have access to all their genetic and medical information."

That knowledge can be a curse—and a blessing. Just ask PGP volunteer number 6, whose sequencing revealed an allele that put him at elevated risk for hypertrophic cardiomyopathy. Church and his colleagues notified the volunteer and recommended that he see a cardiologist for an echocardiogram to determine whether his heart's ventricular wall had begun to thicken, a sign of the disease. On the one hand, such information—or knowledge of a gene that raises the risk of, say, breast cancer or diabetes—may be startling. On the other, it enables volunteers to take action to stave off full-blown disease. That aspect of the project holds particular appeal for Dyson. "The data that the PGP uncovered can help put our health in perspective," she says. "They show that a disease risk doesn't have to be our destiny."

Of even greater value may be the data's promise in advancing the field of personalized medicine. Although pharmacogenetics—the study of how and why specific medications appear to work only in certain populations—is in its early stages, genetic tests have already been developed to help determine which drugs, at what dosages, can help treat certain cancers, HIV/AIDS, psychoses, heart disease, and other conditions. Researchers recently identified, for example, a genetic variant in about 30 percent of people that decreases the effectiveness of the antiplatelet drug clopidogrel, or Plavix; these patients benefit from higher doses of the drug. Ideally, says Church, PGP data will help guide patients and their physicians in treatment decisions.

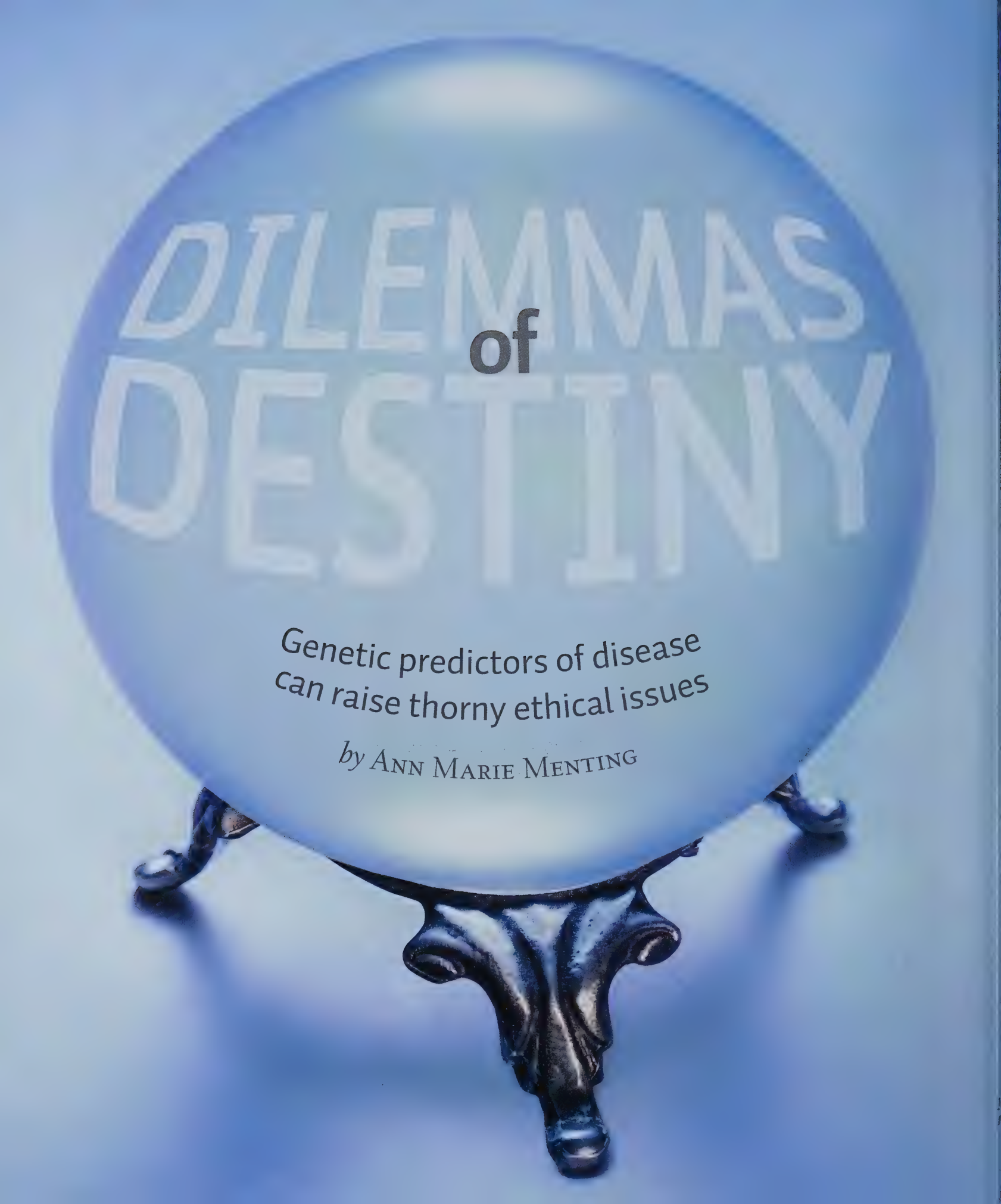
Truth to Power

With the potential benefits of open access come risks. At the top of the list of concerns: the possibility of discrimination by employers and insurers who know an individual's personal genetic information. The Genetic Information Nondiscrimination Act of 2008 has made a leap forward in preventing such issues by making it illegal for employers to make hiring or promotion decisions based on genetic information. The act also bars health plans from charging higher premiums based on genetic information.

Church hopes that as more volunteers join the PGP—the plan is to expand enrollment to 100,000 participants—privacy concerns will fade. He cites PatientsLikeMe, a medicine-meets-social-networking website in which visitors with such conditions as HIV/AIDS, neurodegenerative diseases, and depression share information about themselves and their health. "These used to be very stigmatizing conditions," he says. "Now people see that the benefits of educating others and helping them cope with disease outweigh the hazards of revealing private details. I believe the same thing has happened with the PGP."

Dyson agrees. "The truth," she says, "is never a risk." ■

Jessica Cerretani, a former assistant editor of Harvard Medicine, *is now a full-time freelance writer.*



DILEMMAS of DESTINY

Genetic predictors of disease can raise thorny ethical issues

by Ann Marie Menting

Lila* was only in her twenties when she learned that she could be at increased risk for breast cancer. A genetic test had revealed that her mother carried a mutation signaling a heightened risk for the disease. But Lila opted to live with uncertainty—and the hope it engendered—a little longer. She wouldn't test, but she would be vigilant, opting for frequent mammograms.

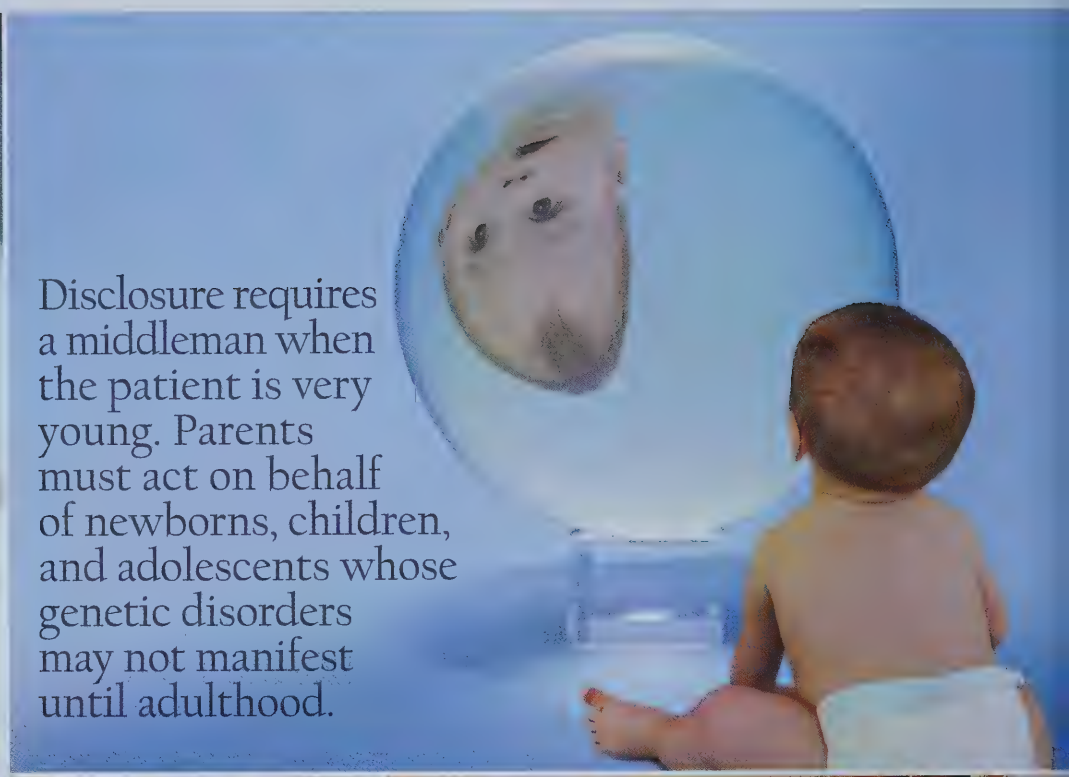
At age 34, Lila, now the mother of two small children, learned she had breast cancer. Personalizing her treatment would require genetic testing. This time she consented. The procedure verified the mutation and revealed another detail: her tumor flourished with exposure to hormones.

"She knew the mutation increased her risk for a second cancer, so she chose bilateral mastectomy," says Judy Garber, an HMS associate professor of medicine at Dana-Farber Cancer Institute and Brigham and Women's Hospital. But because the tumor was hormone-receptor-positive, Lila faced another decision: take drugs to cut her hormone levels, or have the source of those hormones, her ovaries, removed. She chose the surgery.

Garber, who directs the Cancer Risk and Prevention Program at Dana-Farber, describes Lila's decisions as aggressive for a young woman, even one burdened with a mutation promising a lifelong threat of cancer. Could her choices have been driven by her desire to remain a mother to her children for as long as possible?

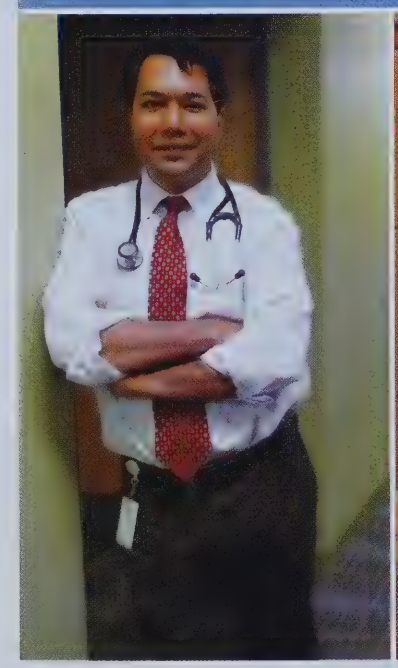
PHOTO: DANIEL SMITH/CORBIS

**The patient's name has been changed.*



GOING FOR THE CODE: Personal genomics receives attention from, clockwise from above: Ting Wu, Kenneth Offit, Judy Garber, and Joseph Thakuria.

Disclosure requires a middleman when the patient is very young. Parents must act on behalf of newborns, children, and adolescents whose genetic disorders may not manifest until adulthood.



"Oh, of course," says Garber, adding softly, "For young mothers, that's often the issue."

Lila's story underscores how genetic diseases thread throughout a family and how decisions made by individuals—to test, to treat, to disclose—are fraught with difficulties and emotions that can strain, and sometimes break, family ties. The reach of genetic diseases goes beyond the individual, often visiting ethical dilemmas upon a patient's entire family.

Over the past three decades, genetic testing and its offspring—personalized medicine—have matured; tests for up to 2,000 diseases are now available. Yet while the ability to identify genetic signposts for patients allows doctors to recommend screening, offer preventive surgeries, and fine-tune drug treatments, that same ability delivers unsettling futures to those with genetic evidence of diseases that as yet have no cure, such as Huntington's disease, cystic fibrosis, hemophilia, and Alzheimer's disease.

Often, patients and doctors become entangled in such issues as how to best share at-risk information, access treatment options, and weigh decisions about hidden threats to the young and unborn. And sometimes these issues mushroom, becoming quandaries for society as a whole.

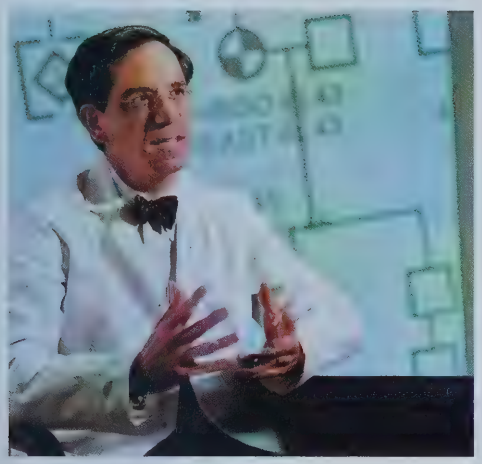
It's a Family Affair

Patients rely on physicians to deliver medical news directly and in confidence, good or bad. Medicine's growing ability to plumb a person's genetic information, however, can challenge this expectation.

"People are accustomed to keeping some details private," says Ting Wu, an HMS professor of genetics and director of the Personal Genetics Education Project. "But genetic information is explicit; it speaks to pedigree."

Wu notes that while patients might seek genetic testing as a means of customizing their treatment and prevention strategies, others—particularly at-risk family members—may be less amenable to testing and the possibility of news of an incurable condition.

"Patients realize that information can sometimes be used in a way that hurts someone," says Wu. "That possibility—and that fear—can present a slippery slope: The more we learn, the more information we have to use, properly or improperly."



How deeply those details penetrate family defenses can be found in a story Wu cites of a 23-year-old woman who chose to be tested for Huntington's disease. The young woman's grandfather had been ravaged by the rare brain disorder for three decades, a maternal aunt had tested positive for it, and she was now witnessing a cousin's debilitation. Her mother, however, refused to test and became embattled with her daughter over the issue. Undeterred, the young women went ahead with her plans. She learned she carried the gene—as did her mother, by implication. Her mother severed their ties, unable to forgive her daughter for inflicting upon them both what she viewed as future-robbing news.

A Fine Line

Kenneth Offit '81, chief of the Clinical Genetics Service at New York City's Memorial Sloan-Kettering Cancer Center, has seen the difficulties that disclosure can bring to families. "When it comes to handling the results of genetic testing," he says, "health professionals must respect the boundaries imposed by the ethical practice of medicine by encouraging, but not coercing, patients to share their news with family members." But when the patient can't meet that responsibility, the custodianship of genetic information—and the duty to warn—may fall to the physician.

"Two decades ago, a breast cancer patient we'd enrolled in a study of the genetic risks of certain cancers died before learning she had a mutation linked to her cancer," Offit says. "We needed to tell her daughters of their own risk—but we didn't know their locations."

Offit called the woman's mother to explain his need to contact her granddaughters. She rejected his plea and ignored his follow-up letter. Years later, after she had died, the daughters found the letter that Offit had written—and showed up at his clinic. One daughter tested positive for the mutation and began regular screening.

Offit once told this story to a group of lawyers to illustrate how he had tried to fulfill his duty to warn. Terse, unsettling comments followed. One lawyer chided him for failing to hire a private detective, find the daughters, and tell them their risks. Another frostily said that, had the daughters developed breast cancer before they were notified, she would have offered to represent them in a lawsuit.

Open House

Physicians aren't the only ones tussling at the ethical edges of genetic testing. Patients, too, wrestle with such dilemmas. They share test results to warn siblings and cousins, help adult children make childbearing decisions, or explain their medical care to others. But patients also withhold information to avoid causing alarm, notifying only those relatives at greatest risk. Information sharing may hit additional barriers, both real and perceived, such as geographic distance, adoption, and stigma.

Disclosure requires a middleman when the patient is very young. Parents must act on behalf of newborns, children, and adolescents whose genetic disorders may not manifest until adulthood. "We often avoid testing children unless it's absolutely necessary," says Joseph Thakuria, an HMS instructor and clinical geneticist at Massachusetts General Hospital. "We worry about how testing can negatively affect this population."

Thakuria, who trains medical students and house staff as well as genetic counselors, says that his worries about stigma and self-concept sometimes begin with the parents. "It's not unusual for one to say to the other, 'It's from your side of the family.' Usually it's said half-jokingly, but I always try to nip that thought in the bud."

He does so by sharing a fact: We are all carriers. Geneticists estimate that each of us has 6 to 25 genes that, under the right conditions, could trigger a disorder or disease in a person or in his or her offspring. Understanding this helps move parents away from shock, guilt, and grief and into proactive postures, such as joining a support group, learning about treatments and interventions, and safeguarding their child's quality of life.

Protective Services

Protecting quality of life for all who undergo genetic testing has gained legal ground in recent years. Worries about institutional discrimination that might deny medical coverage, employment, and equitable access to the benefits of personalized medicine have been eased in the United States by provisions forged in the Genetic Information Nondiscrimination Act, or GINA, and in the recent health care reform legislation.

Since 2008, GINA has accorded genetic information the same privacy protections that the Health Insurance Portability and Accountability Act, or HIPAA, has provided to medical data. GINA has also prohibited genetic discrimination by health insurers and employers.

GINA does not, however, affect life, disability, or long-term care insurance. Nor does it prevent insurers from determining eligibility or rates based on a person's gene-linked disease or disorder that has already manifested. And while GINA mandates payments for tests for mutations linked to diseases such as breast cancer and colon cancer, it doesn't require coverage for preventive interventions.

Health care reforms signed into law in 2010 may help flesh out just what personalized medicine can and can't deliver. The reform act creates an independent Patient-Centered Outcomes Research Institute charged with examining the use and comparative effectiveness of medical products and services within groups differentiated along traditional lines—such as race, sex, and age—as well as new ones distinguished by genetic and molecular characteristics.

Society's acceptance of personal genomics will surface in its laws, says HMS geneticist Wu. Preimplantation genetic diagnosis, for example, which screens for genetic diseases in embryos used for in-vitro fertilization, may come under scrutiny. Studies have found that parents see an advantage to this screening procedure if it means they can avoid receiving a prenatal diagnosis requiring them to consider terminating a pregnancy. But others fear that choosing an embryo based on its genetic makeup is mere prelude to selecting for gender, IQ, and eye color—in short, a slide toward eugenics.

For Wu, education is the right response. "We need to understand the social, legal, and ethical outcomes of our decisions," she says. "When we know the issues surrounding genetic testing, we'll consider carefully before judging the decisions of others. For when we categorize others, we categorize ourselves." ■

Ann Marie Menting is associate editor of Harvard Medicine.

One-Man SHOW

A personal genome pioneer talks about what it means to bare all

Interview by KARIN KIEWRA

John Halamka, a participant in and board member of the Personal Genome Project, was the second person to have his genome sequenced and made public. He is the chief information officer of both Harvard Medical School and Beth Israel Deaconess Medical Center, where he is also an emergency physician. In addition, Halamka oversees the exchange of clinical and administrative data for Massachusetts and serves as chair of the U.S. Healthcare Information Technology Standards Panel.

Why take your DNA public?

Because if you're going to ask what the social, legal, and practical implications of sharing the genome are, somebody has to do it and see what happens. I'm a strong believer that, in the soon-to-be-under-$1,000-per-genome era, we should sequence people at birth and make that data available to help them plan their health care. We already do dozens of newborn screening tests. Why not this?

Any surprises?

I carry a mutation for severe combined immunodeficiency, the boy-in-the-bubble syndrome. So it would be a concern if my daughter were to have a child with someone who also has a family history of that mutation. Otherwise, I'm more susceptible to tuberculosis than the average person. And I'm twice as likely as the average man to develop prostate cancer.

How has this affected your care?

The genome is about probabilities; it's not deterministic. So if I see my PSA go from 0.4 to 2.0, instead of saying, "Oh, that's still in the normal range," I'll say, "Boy, we'd better look at that." My genome helps me think about lifestyle and preventive medicine choices, and then have discussions with my family about health risks. It's been empowering.

After I became a chief information officer at 34, I felt a lot of stress and didn't follow a good diet or exercise regimen. My doctor was ready to put me on Lipitor, beta blockers, you name it. I've since become vegan and shed 70 pounds. What if my genome had revealed to me, at the age of 18, that I was likely to gain weight, develop heart disease, and be at increased risk for a stroke? Maybe I'd have said, "Hmmm. If offered broccoli or a T-bone, I'll choose broccoli."

What else might you learn?

We don't yet know much about how individual mutations actually affect health—by resulting in proteins folding in a unique way, say, and leading to dysfunction. That science is evolving. The real challenge is in relating a given mutation to a disease state or probability. How do I translate a given base-pair change to a change in the architecture of a protein or to the cause

of a disease? That's really hard. How do you turn genomic data into information, knowledge, and wisdom?

The genetic counselors told me, "Here are the implications of what we found in your genome based on the current scientific literature." That will change. A website now exists that allows me to map my data against the latest literature, or what the Personal Genome Project folks have entered into the database as characteristics that might lead to disease. But it's not as though I get monthly emails.

Isn't the Personal Genome Project a family affair?

I have no brothers or sisters. My wife's an only child. So is my daughter. But I do have cousins. I made sure they were all aware of my decision to participate, because my genome could have implications for them.

What about privacy?

In 2005, as part of the Personal Genome Project, I released my genome to the Massachusetts biotech community with my employer and my insurer by my side, pledging publicly not to drop me, no matter the findings. I'm not suggesting that we all share data quite so openly. If your medical record is as boring as mine, the risks of full disclosure are minimal. But what if you had a family history of mental illness, or something else that might diminish your status in the community?

You could get really farfetched. Imagine it's 20 years from now. You walk into a bar where there's a series of USB ports. You plug in a flash drive with your genome on it, and a program highlights all the potential mates you shouldn't approach because if you had kids together, the result would be bad. "Don't chat *her* up. Multiple recessive genes!"

We need to stratify medical records so that you consent to what gets released—and to what purpose. That technology doesn't exist, but we're working on it, along with policies to give consumers greater control.

You have five jobs. What's your goal?

What I care about is the ability to make a difference. I can't think of any institution that has as much technology—and as great an ability to be at the cutting edge—as Harvard. The grass ain't greener anywhere else. ■

TEST CASE: Participation in the Personal Genome Project is not the first pioneering role John Halamka has elected to play in medicine; he has also had a microchip containing his medical records implanted in his arm.

PHOTO: DAVE BRADLEY

IN SEARCH OF SOLACE: The January earthquake reduced to rubble most buildings in Port-au-Prince, including the Cathedral of Our Lady of the Assumption.

PHOTO: JUSTIN IDE/HARVARD NEWS OFFICE

ON THE MEND

Compiled by DAVID CAMERON

HAITI'S HEALTH CARE SYSTEM WAS IN CRISIS—AND THEN THE EARTHQUAKE STRUCK

ONE LATE AFTERNOON IN JANUARY, more than 200,000 people in Haiti died in less than a minute. The 7.0-magnitude earthquake destroyed the infrastructure of this already fragile country, leaving more than a million people without homes, livelihoods, or basic services. ■ For more than two decades, members of the Harvard Medical School community have forged critical partnerships with the people of Haiti. We asked five faculty members who have been intimately involved in the emergency response for their views on how Haiti might regain its footing and how we all might help the country's health care system rise up stronger than ever.

PAUL FARMER

PHOTOS: JUSTIN IDE/HARVARD NEWS OFFICE (LEFT AND RIGHT); COURTESY OF CHRISTIAN ARBELAEZ (BELOW)

THE EARTHQUAKE devastated Haiti's meager health care infrastructure. The only public teaching hospital was nearly destroyed, other medical facilities crumpled, and an entire class of second-year nursing students died alongside their professors when their school collapsed. A week after the earthquake, Haiti's best hospital wasn't even in the country; it was the USNS *Comfort*, floating in the harbor.

In the first few hours and days, we saw mostly surgical disease—gaping wounds, chest traumas, crushed limbs in need of amputation. Harvard and local doctors working as part of Partners In Health were able to help meet these high-volume needs only because we had long-standing partnerships with local public hospitals. Fortunately, most of the employees and facilities that form the core of Partners In Health's efforts to provide health care to Haiti's rural poor were outside the earthquake zone.

Even before the earthquake, Haiti's health care system lacked the capacity to care for patients with surgical disease. On average, people in the United States have half a dozen surgical procedures in their lifetimes; Haitians tend not to have *any*. Yet, between this excess and scarcity lies a middle ground.

My colleague David Walton '03 is currently overseeing a Partners In Health joint effort with the Ministry of Health and other collaborators to build a national teaching and reference hospital in central Haiti; its structure will conform to California earthquake standards. With six operating theaters, the facility will be Partners In Health's largest project in two decades.

Right now, though, the situation in Haiti is grim. More than a million people are displaced in camps, some of which sprang up in the very places that need rebuilding. People need shelter. Rains and winds can easily sweep away their tents; you don't need a hurricane to bring down a tarp.

The only way to rebuild sensibly and ethically is to provide temporary settlements that meet basic needs, such as electricity and running water. Decent jobs are also vital. Public works, reforestation, and watershed protection projects could easily employ a million Haitians. There's no dearth of work to be done and no dearth of resources. But what's critical right *now* is getting the resources into the hands of the people who need them most. ■

Paul Farmer '90, PhD, chair of the HMS Department of Global Health and Social Medicine, cofounded Partners In Health.

CHRISTIAN ARBELAEZ

I ARRIVED IN HAITI two weeks after the earthquake, immediately after the first team rotated out. From Port-au-Prince, we traveled 90 minutes on a semi-paved road to Saint-Marc, a town of just under 200,000. There we found St. Nicolas Hospital, a collection of single-story buildings, busting at the seams with patients. Amid an influx of transferred patients, we ran the operating rooms, staffed the emergency department, and performed patient rounds, all while improvising with makeshift solutions, such as using masking tape to number the beds and craft patient wristbands.

For ten days, I worked as the only emergency medicine specialist with a team of surgeons, orthopedic surgeons, anesthesiologists, and nurses in

LIFE AND LIMB: With estimates of earthquake-related amputations surpassing 100,000, Haiti must provide care for a generation of amputees.

A WEEK AFTER the earthquake, Haiti's best hospital wasn't even in the country; it was the USNS *Comfort*, floating in the harbor.

—PAUL FARMER

chaotic conditions. Together with our Haitian colleagues, we treated more than 500 patients needing wound care, amputations, skin grafts, and pain alleviation. We also dealt with routine emergencies like childbirth, trauma, and acute exacerbation of chronic conditions.

My stint on the front lines left a deep impression of how much remains to be done in Haiti. We need to place a priority on shoring up the country's devastated medical infrastructure. This involves a critical examination of its medical and nursing education and training systems. In addition, to sending U.S. health care providers to provide ongoing relief, we need to think about rebuilding the country's capacity and train local community health workers to tackle top public health priorities.

Less obvious to many people is the profound psychological toll that Haitians will be grappling with for years to come. Most surviving trauma victims suffered limb-threatening injuries, creating a need for prosthetics, ongoing orthopedic care, and rehabilitation. The discrimination and social stigma that comes with this vulnerability—along with the consequences of widespread post-traumatic stress disorder—will demand comprehensive psychological treatment. Rebuilding Haiti will require the hope, resilience, and strength of the Haitian people as well as the long-term commitment that the world has promised. ■

Christian Arbelaez, MD, MPH, is an HMS assistant professor of medicine at Brigham and Women's Hospital.

PEOPLE DON'T simply live in Haiti; they *survive* in Haiti. To help Haiti, we must think about children born after the earthquake.

—CLAIRE PIERRE

CRI DE COEUR: Confusion and fear spawned by the quake complicated the already fragile lives of many Haitians.

DAVID WALTON

THE EARTHQUAKE'S damage to the General Hospital in Port-au-Prince was breathtaking. In Harvard terms, imagine what it would be like if not just the medical school but also the entire university and all the affiliated hospitals were lost—gone in an instant, along with all the people who worked at those institutions.

Immediately after the earthquake it was my role to coordinate the work of nongovernmental organizations with the General Hospital. With only part of the hospital still standing, most medical care took place in tents. To address the initial shortage of Haitian orthopedic and trauma surgeons, we reached out to HMS faculty. The response was tremendous. Dozens of Harvard physicians and nurses provided on-site aid in those critical first few weeks.

Before the earthquake, the Haitian Ministry of Health had asked Partners In Health to build a community hospital in central Haiti to serve an area with roughly 160,000 inhabitants. Since medical infrastructure is a specialty of mine, I was overseeing that project. Then the earthquake hit—and changed our plans in two ways.

First, because the now-disabled General Hospital in Port-au-Prince had been the major teaching hospital for the entire country, we were asked to redesign the new hospital for education. We increased ward space, added a second floor, and changed our overall design to accommodate teaching for medical students, nursing students, and resident physicians. Second, we were asked to enlarge the hospital to 180,000 square feet to make room for 320 beds, six operating rooms, an intensive care unit, an endoscopy suite, and women's health and ambulatory care units.

We broke ground for the National Teaching Hospital in Mirebalais this past summer. We'll soon have the main buildings well under way, and by late spring we'll be installing equipment. We hope to accept patients by the end of 2011. Even though this will be Haiti's state-of-the-art hospital, it will only begin to address the country's medical needs. After all, 320 beds must serve hundreds of thousands of people. Haiti needs several dozen such hospitals. ■

David Walton '03 is an HMS instructor in medicine at Brigham and Women's Hospital and deputy chief of mission for Partners In Health.

CLAIRE PIERRE

WE ARRIVED IN Haiti three days after the earthquake to find a scene of unimaginable suffering and chaos. As one of the first on-site medical personnel, I provided triage for clinical and surgical teams—usually through the night. As a Haitian citizen, I witnessed my country's loss not only of physical structures, but also of human capacity.

After those first few horrifying days, I went on to collaborate with nongovernmental organizations and major donors to assist government officials with triage. More than ever, Haiti needs partners, groups, and individuals able to commit to long-term reconstruction efforts. While it is obvious that my country needs a whole new health care system, it also cries out for a new educational system and a revamped economic infrastructure.

One lesson the earthquake taught us is that, for Haiti, decentralization is key. But such decentralization will require an expansion of training opportunities. To open a rural, locally run clinic, for instance, would require not only recruiting Haitian doctors, but also training secretaries, administrators, maintenance workers, and custodians.

Haiti is home to wonderful nongovernmental organizations—more than most developing countries. Without them, many people would not receive care. But these organizations take a patchwork approach—one that has achieved some fascinating and in many cases lifesaving projects yet has failed to build a core of fundamental services.

In one area, organizations raised money to build schools—complete with sports programs—up to the sixth grade. Yet no high school exists because fundraising for adolescents has proved so much more challenging than fundraising for young children. Such gaps compromise Haiti's long-term stability.

By diversifying their interests and partnering with the public sector rather than creating separate, parallel structures, those organizations could provide more children with access to the basic services they need to grow into productive citizens.

People don't simply live in Haiti; they *survive* in Haiti. To help Haiti, we must think about children born after the earthquake. How can we give them opportunities to thrive? We shouldn't just look at a Haitian child as someone to help, but as someone who will one day become the helper. ■

Claire Pierre, MD, is an HMS instructor in medicine at Cambridge Health Alliance.

JOIA MUKHERJEE

I CAN'T OVERSTATE the horrors that occurred when the earthquake struck or the dire needs that remain. After all I witnessed it took me months before I could sleep through the night.

In the aftermath, I spent much of my time coordinating Partners In Health's efforts to bring health services to people displaced or subsisting in camps, where infectious diseases and other health problems have been overwhelming. By coordinating our efforts, we were able to partner with both local community groups and the Haitian government.

These camps are enormous, with populations often surpassing 50,000 people. To provide medical care at such epic proportions and under such difficult conditions, we hired Haitian doctors and nurses who were suddenly unemployed. Essentially, we hired displaced medical personnel to help displaced people.

In rebuilding Haiti, one area that demands attention is medical education. Most of the volunteer physicians and surgeons we recruited were from academic medical centers. Drawing on the expertise of HMS faculty members as both doctors and educators could provide a major boost to medical education in Haiti.

We envision creating a primary-care residency program there that involves recruiting physicians from Harvard and elsewhere to train Haitian doctors. Ideally, we'd like to start with a residency program—a collaboration among HMS, other U.S.-based universities, and the now nearly decimated National Medical School in Haiti—to train a dozen Haitian doctors a year. Remember that before the earthquake, Haiti had one doctor for every 11,000 people. With proper funding, this program would have an enduring impact on Haiti's reconstructed medical infrastructure. ■

Joia Mukherjee, MD, is an HMS associate professor of medicine at Brigham and Women's Hospital and chief medical officer for Partners In Health.

EYES ON THE SKIES: Space entrepreneur Peter Diamandis turned to racing rockets when he found racing cars to be dull.

How to Race Rockets

PHOTO: GREGG SEGAL

Seeking expert advice on radiant skin, rejuvenating slumber, **and other practical** quests? Hankering instead for odd **and impractical tips**, such as how to nab a serial killer using discarded pizza, transform your name into a verb, or coax a mummy into spilling its guts? Read on for some professional insights **from Harvard doctors.**

How to Race Rockets *by Peter Diamandis*

tips

The sky has always fueled my dreams—and led me to launch more than a dozen spaceflight companies. The Rocket Racing League, my latest venture, will debut with demonstration races in 2011. Starting its engines has taught me a few lessons about racing at rocket speed.

Let boredom inspire you. I got the idea for the Rocket Racing League several years ago while racing an Indy car. After a few laps, I realized I was bored. Racing on an earthbound track, grounded by gravity, just didn't thrill me. It would be so much more fun, I thought, if the track could be three-dimensional. If the vehicles resembled the pod racers from *Star Wars*, we could bullet into the sky or swoop down through hoops. The idea stuck with me, and I teamed up with racecar experts to start the league. It's since been christened "NASCAR with rockets."

Start with one foot on the ground. Working with top avionics companies that design fighter jets, we've developed a rocket-powered vehicle that's fueled by liquid oxygen and ethanol. Now we're adding a three-dimensional virtual racetrack so pilots can zoom through rings and gateways.

Tap your inner child. My passion for space flight started midway through the Apollo program, when I was nine. With the Rocket Racing League, we've tried to recapture that sense of awe by aiming to inspire people in the cockpit and on the ground. Spectators can play along—and even compete with the pilots—by viewing the pilots' superimposed three-dimensional racecourse from the stands or at home through their television sets or computers.

Be built for speed. Rocket racers include some of the best acrobatic, military, and test pilots in the world. Some are racecar drivers who also fly. I'm a pilot, and I will absolutely race.

Accept a virtual reality. Races will take place on a racecourse two miles long, one mile wide, and 1,500 feet in the air. A typical race will take about an hour; fans will be able to watch from multiple camera views, including the cockpit. When pilots miss a ring or gateway on the three-dimensional racetrack, the resulting explosions will be virtual. Their rockets will be real, however, so each racer will follow a separate track to avoid collisions.

Forget *Star Trek*. In designing the races, we've been careful to avoid engineering inaccuracies. My favorite *Star Trek* blunder? That swooshing sound the *Enterprise* makes when accelerating through deep space.

ROCKET SCIENCE: As a medical student, Peter Diamandis would haul a brick-sized cell phone on patient rounds so he could monitor NASA's test firings of rockets.

PHOTO: GREGG SEGAL

Peter Diamandis '87 is cofounder and chairman of the Rocket Racing League; chief executive officer of the X PRIZE Foundation, a nonprofit that conducts technological competitions; cofounder and director of Space Adventures, which brokers the flight of paying citizens into orbit; and chief executive officer of Zero Gravity Corporation, which offers weightless flights.

How to Nab a Serial Killer

by Frederick R. Bieber

For more than two decades, the Grim Sleeper had stalked the streets of Los Angeles, brutally murdering at least eleven people. He left his DNA—but without a match in convicted-offender databases, police were stymied. Then, in July 2010, DNA from a discarded pizza crust led to the arrest of a suspect. A new tool, known as familial DNA searching, had identified him through a partial match to his son, whose DNA profile was in California's convicted-offender database. Familial searches of DNA databases—and, in some cases, lunch remnants—hold great promise for unlocking even the most enigmatic crimes.

Explore family ties. I've worked with several teams to identify victims of mass disasters and war—including those who died in the September 11 terrorist attacks and in Hurricane Katrina—using DNA from their relatives. These experiences triggered a eureka moment for me: Why not use these powerful kinship tools to search for possible suspects in criminal investigations?

Build a genetic library. Familial searching methods have been used to solve crimes in England, where DNA samples are taken upon arrest for most offenses and the profiles saved in a large, searchable database. In 2006 I coauthored a *Science* paper illustrating the power of kinship analysis for indirectly identifying criminal suspects. We estimated that this approach could increase the "cold-hit" rate—the chance of matching a crime-scene sample with a suspect—by 40 percent. In 2008, California became the first state to approve an official policy for familial DNA searching; two years later the Grim Sleeper investigation became the first California case to employ this method.

Engage in the debate. Despite successes here and abroad, familial DNA searching isn't without controversy. Critics argue that the process invades the privacy of criminals' relatives. Yet most of the work happens behind the scenes, with relatives rarely contacted. Moreover, familial DNA—a valuable tool for identifying missing persons and determining paternity—is increasingly used to exonerate the innocent. Used judiciously, this technique can help shed light on some of human nature's darker mysteries. ■

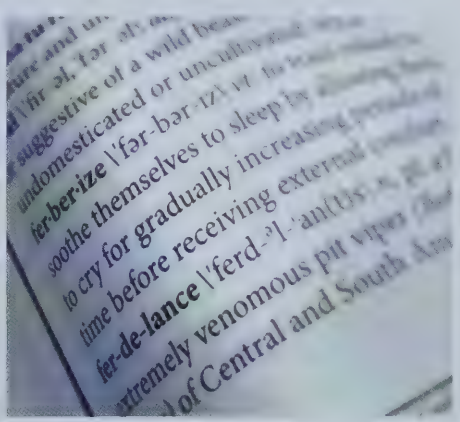
Frederick R. Bieber, PhD, is an HMS associate professor of pathology at Brigham and Women's Hospital.

How to Become a Verb *by Richard Ferber*

I never set out to be a verb—and certainly never hoped to be one. I'm not sure when the term *ferberize* crept into the country's lexicon. It seems to refer to a method for helping children learn to fall asleep under the same unchanging conditions they'll encounter through most of the night—just one of many techniques we use in the Center for Pediatric Sleep Disorders at Children's Hospital Boston. This oversimplification has forced me to learn several lessons about becoming a verb, some of them cautionary.

Apply early. When we began our work in 1978, no other centers were tackling children's sleep problems comprehensively. Myths, knee-jerk recommendations, and inappropriate prescriptions prevailed. Today, though, clinicians and researchers worldwide focus on children's sleep, and physicians are better able to understand normal sleep patterns, recognize the sources of problems, and design rational strategies for solving those problems.

Be willing to be misunderstood. A downside to becoming a generonym—a proper noun used generically, such as Band-Aid, Kleenex, and Xerox—is that you have no control over the usage. The verb



ferberize—and its noun companions, such as "the Ferber method"—inaccurately distills decades of our work into a single, simplistic concept. *Ferberizing* seems to imply that sleep problems carry a one-size-fits-all solution: forcing babies to cry themselves to sleep, a technique we oppose.

Roll with the punchlines. Movies and television programs occasionally spoof the term *ferberize*. I've learned to ignore the references and even join in the laughter.

Have a surname that's easily converted. Two-syllable names ending in "er" are best, as they easily accommodate the addition of "ize" or "ism." For all those Millers, Parkers, and Fliers—there's hope for you yet. ■

Richard Ferber '70, an HMS associate professor of neurology at Children's Hospital Boston, is the author of Solve Your Child's Sleep Problems: New, Revised, and Expanded Edition *(Fireside, 2006).*

PHOTOS: KONSTANTIN PAPADAKIS/ISTOCKPHOTO.COM (ABOVE); MATTIAS PALUDI

tips

How to Deploy an Emergency Medical Team

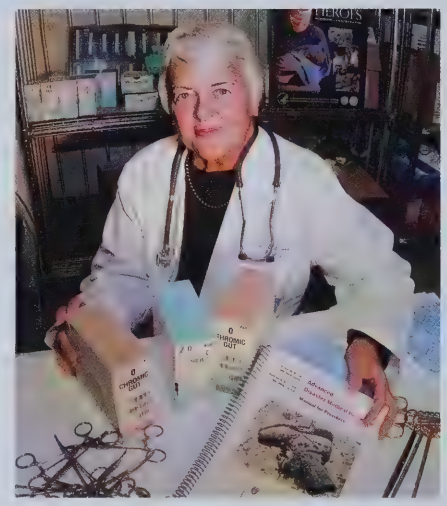
by Susan Briggs

Preparing to dispense a medical team to care for victims of natural and man-made disasters starts well before you receive a call announcing a calamity.

Muster your troops. Ninety percent of disaster response is being prepared for a disaster. The most important step is gathering in advance a complement of medical professionals. Our Boston-area volunteers, part of the U.S. government's International Medical Surgical Response Team, or IMSuRT, number around 250. When activated by the government, 50 of these IMSuRT members deploy with a fully equipped field hospital.

Prepare those troops. Volunteers for federal disaster teams must be current with their immunizations and federalized in advance, which requires them to pass security checks and obtain special passports. Team members must also cultivate a "readiness mentality"; they must be endlessly inventive, instantly adaptive, and entirely self-reliant.

Be ready to go. Keep trucks stocked with supplies, generators, and other equipment. Have pharmaceuticals and units of blood available on-call. Instruct volunteers to keep suitcases packed at all times with antidiarrheal medications, antibiotics, anti-inflammatories, work boots, long-sleeved shirts, bug spray, mosquito nets, toilet paper, candy bars, and coffee.



READY FOR ACTION: Susan Briggs keeps her bag packed for any disaster.

Establish response systems. When a request-to-deploy call comes in, IMSuRT team members must be ready to depart within six to eight hours. Rapid notification of volunteers through email and by pager is the first priority, as they need time to ensure that their patient and family responsibilities are covered.

Sustain team members' spirits. The psychological toll on volunteers can be high. They work in stark conditions without stop, and all too often they must triage severely injured patients for nothing more than palliative care. Emphasize self-care and remind team members that their colleagues are their best support.

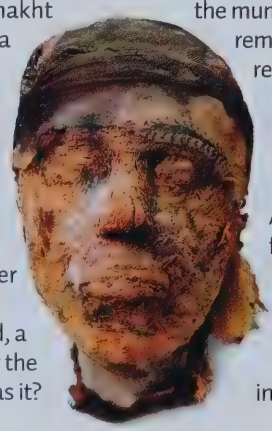
Susan Briggs, MD, founder of the International Medical Surgical Response Team, directs Massachusetts General Hospital's International Trauma and Disaster Institute.

How to Unwrap the Secrets of a Mummy

by Rajiv Gupta

Find a mummy. In 1915, a joint expedition of Harvard University and the Boston Museum of Fine Arts found mummified remains in the burial chamber of Djehutenakht ("Jeh-HOO-teh-nocked"), a governor in Egypt's Middle Kingdom, and his wife.

Lose the body (not recommended). At some point in the previous 4,000 years, the chamber had been looted, with one mummy stolen and the other dismembered. The 1915 expedition uncovered a head, a torso, and a finger; now only the head remains. But whose was it?



Look closer. We scanned the head at Massachusetts General Hospital's ultra-high-resolution volume CT lab in preparation for extracting dental DNA to determine the mummy's gender. The genetic testing remains inconclusive, but our scans revealed some surprises.

Follow the fractures. The scans showed broken and missing facial bones where the jaw muscles would normally attach. At first we suspected damage from looting, or a side effect of excerebration, the process by which embalmers removed the brain. But the embalmers had made purposeful, precise cuts from inside the mouth. Why bother?

Get literal. Ancient texts describing a rite called the Opening of the Mouth cited a chisel, but researchers had long assumed that the tool related to a statue and the opening was symbolic. Then we wondered: What if the authors had meant a literal opening? What if, in an effort to enable the deceased to speak in the afterlife, the embalmers had operated to let the jaw open freely, despite rigor mortis?

Do it yourself. To test our theory, we prevailed on maxillofacial surgeons to perform the jaw-dropping procedure on cadavers with tools similar to those the ancient Egyptians used. Our preliminary findings suggest that the embalmers indeed honored the ancient rite to ensure the mummy's freedom of speech well into the afterlife.

Rajiv Gupta, MD, PhD, is an HMS instructor in radiology at Massachusetts General Hospital.

PHOTOS: JOSHUA TOUSTER (ABOVE); COURTESY OF *THE AMERICAN JOURNAL OF NEURORADIOLOGY*

How to Get a Good Night's Sleep

by Elizabeth Klerman

Why do we sleep? For decades, sleep researchers have been trying to understand why we spend a third of our lives sleeping. What we have found is that slumber not only makes us feel alert and refreshed, but also fulfills vital physiological functions. Our bodies need sleep to aid our metabolic and immune systems, to create and retain memories, to boost mood, and to fortify judgment. But in today's fast-paced world, how can you get a good night's sleep?

Follow a regular sleep-wake pattern. Help regulate your internal clock by going to sleep and waking at the same time each day. Avoid altering your hours on weekends, as even minor shifts can mimic jet lag.

Adhere to a bedtime routine. Your body needs signals to prepare to sleep, such as washing your face or brushing your teeth. Try reading a book in muted lighting to help you unwind.

Avoid eating, exercising, discussing work, or watching television right before bedtime. These activities may act as stimulants.

Maintain a sleep-conducive environment. Keep your bedroom quiet, dark, and cool at night, and use it for sleep, sex, and soothing prose only; it is *not* the place to watch horror movies, pay bills, or check emails.

Temper caffeine and alcohol consumption. Both can disturb sleep. Abstain from caffeine starting at least four hours before bedtime; it can stay in your system for as long as twelve. Do not consume alcohol in the three hours before bedtime. Although alcohol may induce drowsiness initially, it can cause increased wakefulness in the middle of the night once it metabolizes.

Toss the blackout shades. Circadian rhythms adjust to light changes; use those natural cues to your advantage.

Don't stint on sleep. Most adults need eight hours to function optimally. Chronic sleep deprivation leads to decreases in performance, alertness, cognition, and motor skills, while also increasing the risk for such health problems as prediabetic conditions, immune deficiencies, cardiovascular disease, and mood disturbances. Nationally, sleep deprivation accounts for an estimated 100,000 auto accidents and more than 1,500 fatalities each year.

Enlist professional help when all else fails. If you suspect a sleep disorder or consistently do not feel refreshed after eight hours of sleep, consult a sleep specialist. ■

Elizabeth Klerman '86, PhD, is an HMS associate professor of medicine and an associate physician in the Division of Sleep Medicine at Brigham and Women's Hospital.

DREAM A LITTLE DREAM OF EWE: Want to ensure a restful night? Count caffeine-free hours, not sheep.

PHOTO: STICKYSEN/STOCK.XCHNG

How to Perform Magic for Kids

by Eric Zwemer

CASTING A SPELL: Medical student Eric Zwemer enchants five-year-old Elichannel with a series of magic tricks in her room at Children's Hospital Boston.

Magic can be a wonderful distraction, especially for hospitalized children. With a little practice—and simple props—you too can become a caring conjurer. Here's one of my favorite tricks, a variation on the classic saw-the-magician's-assistant-in-half trick that you can easily perform at a child's bedside.

The envelope, please: In advance of the performance, seal an envelope, then snip off its ends to create a hollow tube. Squeeze on the folds of the envelope and gently flatten it. Cut two slits in the back of the envelope several inches apart, then smooth the envelope back into its original shape.

Now, the magician's assistant: Cut a full-length silhouette of a man or woman from a magazine, or print the doctor image we've provided on the *Harvard Medicine* website, taking care to ensure that the figure is longer than the envelope. In a pinch, simply cut a long strip of paper and draw a stick figure on it. You can even ask the child to do the drawing.

The performance: Show the paper figure to the child, then slide it into the envelope, keeping the side with the slits facing you. As you slide the figure in, thread it outside of the envelope through the first slit and back in through the second. Keep up a patter to distract the child. Then, while holding the envelope by the top with one hand, cut the envelope in half with the other, ensuring that the scissor blades stay between the envelope and the figure.

The reveal: After you've finished snipping the envelope, slide the figure out to show, with great flourish, that it survived the operation intact! ■

Eric Zwemer '11, a fifth-year student at HMS, has performed magic for children with life-threatening illnesses since his college days. For additional tricks and the doctor image, visit harvardmedicine.hms.harvard.edu/tips/magic.php.

tips

PHOTOS: SUZANNE CAMARATA (ABOVE); MATTIAS PALUDI

How to Get Ready for Your Closeup

by Jessica Wu

As part of my dermatology practice in Los Angeles, I've prepped many famous faces for red-carpet and on-camera appearances. For Hollywood celebrities, whose faces appear on screens large and small, having healthy, flawless skin is essential. To help them unlock that starlit glow, I coach my celebrity patients to use the same simple skin-care regimen that I offer all my patients. Those same tips can help you shine in Hollywood style for your upcoming photo shoot or special event.

Just add water. Care for your skin from the inside out starting at least two weeks before an event. Hydration is key. Drink plenty of water and avoid the dehydrating effects of caffeine and alcohol. This tip is especially important in the winter months, when lower humidity and dry heat can cause your skin to lose up to 25 percent more moisture than during the warmer months.

Feed your face. Incorporate omega-3s into your diet every day to replenish fatty acids and keep your skin soft and pliable. Try natural sources of omega-3s—such as salmon, sardines, mackerel, walnuts, flaxseeds, and tofu—or take omega-3 supplements.

Shed the dead. Dry flakes dull your skin and magnify wrinkles. Instead of accentuating these unbecoming features, shed some skin. Scrubbing off dead layers will help your face reflect light beautifully for the camera. I recommend exfoliating twice a week—or once a week for sensitive skin. And don't forget your body, especially if you're planning to bare some skin.

Keep it simple. Don't go overboard with skin-care products; using too many can cause skin irritations and breakouts. Products that serve multiple functions—such as a combination moisturizer and sunscreen—are good solutions.

Fake a glow. I confess that I prefer a sun-kissed glow. Luckily, bronzers and tinted body lotions can generate a soft, healthy radiance without risk of sun damage or skin cancer. Actually, this is a time-honored Hollywood secret: celebrities often hide pale complexions beneath bronzers and tanning lotions. ■

Jessica Wu '93, an active voluntary clinical professor of dermatology at the Keck School of Medicine at the University of Southern California, also maintains a private practice in Los Angeles.

How to Patch Up a Rodeo Clown

by Mark Adickes

Bull riding has been called the most dangerous eight seconds in sport. Even my years as an offensive lineman in the National Football League couldn't have prepared me for the rough-and-tumble world of the rodeo. Now, as team physician for the Houston Livestock Show and Rodeo, I patch up not only cowboys, but also tough-as-nails rodeo clowns, who are just as likely to become unstitched.

Send in the clowns. Rodeo clowns—also known as bullfighters—are the first line of defense in the ring. When a rider is bucked off or jumps, the clowns run in to try to divert the bull. Their colorful makeup and clothing belie the dangers they face, and the padded vests they wear beneath their costumes provide only limited protection.

Be a good sport. Most rodeo physicians stand in the ring, ready to scramble over the fence when a nearly one-ton bull charges. Because of my old football injuries, I wait behind the fence and enter the ring only to provide treatment. Naturally, my caution has led to some ribbing about being a football player who's afraid to face bulls.

Stitch in time. As soon as the animals have cleared the ring, I rush in to evaluate the athletes. Under pressure not to delay the show, my team assesses injuries quickly. Whenever possible, we treat the cowboys and clowns immediately, and we even suture lacerations right in the stadium.

Treat the back-in-the-saddle-too-soon syndrome. Rodeo cowboys and clowns are the toughest athletes on the planet. Contusions and lacerations are their most common injuries, but we have also treated ACL tears and femur, facial, and rib fractures. Most of these guys don't make a dime if they don't compete, so they're anxious to get back in the saddle. I've witnessed cowboys competing with bicep ruptures, wrist fractures, and serious back spasms—injuries that would sideline jocks in other sports. We had to physically restrain one cowboy with a fractured thighbone. He kept saying, "Let me get up, man! I can walk this thing off." ■

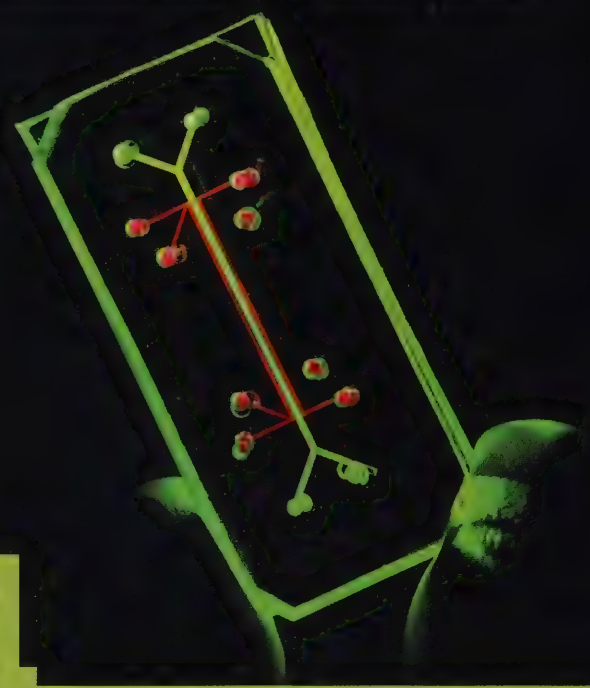
Mark Adickes '00 is the team physician for the Houston Livestock Show and Rodeo, the Houston Rockets, and the U.S. Ski Team. He is also a co-medical director and orthopedic surgeon at the Memorial Hermann Sports Medicine Institute in Houston.

SMART SCIENCE

THE FUTURE OF MEDICINE IS NOW

Organ Recitals

Harvard Medical School researchers work at the intersection of biology and engineering to fashion and adapt artificial organs for use in humans.



1

Microscopic Breathing

RESPIRATION MOVES OXYGEN across lung membranes into the bloodstream and, in reverse, flushes carbon dioxide from the body. Inhaled particles, drugs, inflammatory molecules, and even cancer cells traverse these delicate barriers. In an effort to mimic what occurs naturally, scientists at Harvard's Wyss Institute for Biologically Inspired Engineering have created an artificial lung-on-a-chip by layering cells that line human lung airsacs and blood vessels on a porous, flexible membrane. This translucent device, roughly the size of a rubber eraser, induces the membrane and cells to expand and contract under vacuum pressure to imitate breathing; air flows on one side of the membrane, while fluid containing human immune cells flows on the other. The miniature lung mimics the way tissue absorbs nanoparticles and bacteria—and the resulting immune responses or toxic reactions, says Donald Ingber, founding director of the Wyss Institute and the project's leader. The device could reduce reliance on animals as research subjects, Ingber says, and cut the time and costs involved in bringing new drugs to market.

Cells that Beat as One

HOW DO YOU MAKE HEART TISSUE out of a single cardiac cell in a Petri dish? The answer, it seems, is geometrical. In biology, form dictates function, says Kevin Kit Parker, a faculty member at the Wyss Institute. By designing minute scaffolds to control their geometry, Parker can prod cardiac cells to join together and create tissues that mimic those in a beating heart. Parker's approach draws from the natural process of self-assembly, which, in this instance, allows cells to aggregate into functional systems by responding to "architectural" cues from their surroundings. In proof-of-principle findings this past year, Parker and his collaborators created a layer of beating heart tissue that can transmit electrical impulses. "Emergent needs for this technology are to engineer tissues useful for drug discovery and safety screening," says Parker. In the future, he adds, doctors will likely replace damaged heart valves with engineered tissues and implant tissue-engineered pacemakers that don't need batteries.

2

A Revamped Septic System

SEPSIS, A SYSTEMIC INFECTION, can throw the body's immune system into overdrive, causing widespread damage to organs and tissues. If left unchecked, the condition can prove fatal for young children and anyone with a compromised immune system. Researchers at the Wyss Institute and Children's Hospital Boston have developed an artificial spleen that can be used to treat sepsis. Just as dialysis clears the blood of wastes, this microengineered device clears pathogens from blood that has been infused with tiny magnetic particles. These particles, coated with opsonins—binding molecules naturally found in blood—latch preferentially onto bacteria and other foreign invaders. A magnetic field in the artificial spleen then traps the particles and their tethered pathogens, effectively removing the pathogens from the body. Cleansed blood, meanwhile, flows back into the patient through a catheter, according to the Wyss Institute's Donald Ingber. "We're scaling up to the point of being able to clean hundreds of milliliters of blood per hour," Ingber says, "and we believe that we can increase this capacity even further."

IMAGES: COURTESY OF THE WYSS INSTITUTE FOR BIOLOGICALLY INSPIRED ENGINEERING (1 AND 3); IBRAHIM DOMIAN (2); SEBASTIAN KAULITZKI/ISTOCKPHOTO.COM (4)

4

Attached at the Hip

MANY PEOPLE WITH type 1 diabetes endure regular finger-stick blood tests and insulin shots as they try to keep levels of blood glucose within the normal range. To help them avoid this routine and achieve better blood glucose control, scientists at Massachusetts General Hospital and Boston University are testing an artificial pancreas that regulates glucose continuously and automatically. Worn on a belt like a cell phone, the device takes glucose readings every five minutes from a tiny sensor inserted about an eighth of an inch under the skin. It then administers precise doses of insulin and another important hormone, glucagon, to match physiological demands. In a small clinical trial led by HMS Instructor in Medicine Steven Russell, the re-invented pancreas regulated glucose successfully. Now researchers are testing the device's ability to keep glucose levels stable during exercise, when muscles turn glucose into energy. *—Charles Schmidt*

ASSEMBLY INSTRUCTIONS
HOW TO BUILD A BETTER DIET

FIRST, FORGET THE WORD *diet*. The new buzz is that we don't diet to lose weight; we eat smart to live long and well. David Eisenberg '80, the Bernard Osher Associate Professor of Medicine at HMS, believes that one route to persuading the general population to eat well is to teach health professionals how to cook smart. So each spring Eisenberg hosts Healthy Kitchens, Healthy Lives, a conference in Napa Valley. This collaboration between Harvard Medical School and the Culinary Institute of America aims to improve what Eisenberg calls the culinary literacy of health care professionals. "Doctors' diets are no better than that of the average American," he says. "But if we learn to cook smart and eat smart, we can model a healthful diet for our patients."

—*Louisa Kasdon*

1 Get Cooking

Master basic healthful cooking techniques. Learn how to chop and chiffonade, to stir-fry and steam, to bake and broil. Invest in quality knives and good pots and pans. Buy cookbooks that inspire you. Watch a cooking show or, better yet, take a hands-on class. The more enthusiastically you delve into the culinary arts, the more likely you are to develop a healthful approach to food.

2 Maintain Perspective

Even healthy eaters sometimes overeat. Rethink the portions on your plate, eat slowly, and stop when you're full. Remember that a three-ounce serving of protein, which is ample, is the size of a deck of cards.

3 Get the Whole Story

Avoid heavily processed foods and those with a high-glycemic index. Learn to love nutrient-packed whole grains, such as brown rice and quinoa. Try kasha and kamut, and switch from white bread and white pasta to whole-grain bread and enriched wheat pasta. Incorporate legumes, seeds, and nuts—think peanut butter and hummus—into your daily diet. Choose sweet potatoes instead of white potatoes; opt for whole fruits rather than fruit juice. Toss a cup of left-over vegetables into sauces and soups.

4 Chew the Fat

All fats are not created equal, and research shows that low-fat diets do more harm than good. Rather than trying to banish fats from your diet, cook and flavor your food with high-quality plant oils, such as canola, sunflower, and olive oil.

5 Go Fish

Substitute a seafood dish for meat at least twice a week. Your heart will benefit from the extra boost in omega-3s; research suggests that eating just six ounces a week of fatty fish, such as salmon or sardines, may be enough to reduce your risk of dying from heart disease by 36 percent. You can also aim for the prescribed daily minimum of 250 milligrams of omega-3s by sprinkling a handful of walnuts or flaxseeds on your salad.

6 Chase a Rainbow

Each day, at every meal, eat something colorful: fruits and vegetables in red, orange, yellow, dark green, or blue. The deeper the color, the higher the nutritional value. Diets rich in fruits and vegetables can decrease your chances of having a heart attack or stroke, protect you against some types of cancers, lower your blood pressure, and help ward off cataracts and macular degeneration. Pick at least one day of the week to eat vegetarian. And remember that no single fruit or vegetable provides all the nutrients you need for good health; variety is key.

7 Think Globally

Discover new flavor combinations by sampling traditional fare from around the world. Many cuisines, from the highly touted Mediterranean diet to a range of Asian and Latin American gastronomies, represent rich, delicious sources of inspiration for cooking with fruits, vegetables, whole grains, legumes, and nuts—foods that should be emphasized in any healthful diet.

ILLUSTRATION: WESLEY BEDROSIAN

FIVE QUESTIONS FOR ATUL GAWANDE

Name: Atul Gawande '94, MPH

Roles: Surgeon, Brigham and Women's Hospital; Associate Professor of Surgery, Harvard Medical School; Associate Professor in Health Policy and Management, Harvard School of Public Health; Director, Global Challenge for Safer Surgical Care, World Health Organization

Latest Book: *The Checklist Manifesto: How to Get Things Right* (Metropolitan Books, 2009)

Your latest book, *The Checklist Manifesto*, examines the role of the checklist in the operating room. Can a humble checklist really save lives?

Though it seems almost ridiculous in its simplicity, we've found that a checklist *can* save lives. And two recent studies—in the Veterans Administration system and in the Netherlands—have confirmed the substantial mortality reductions we observed when teams are trained in the principles the checklist embodies. What's intriguing are those principles. Checklists are memory aids. But, designed well, they also foster teamwork. Doctors don't love to use them at first. I know I didn't, and I was running the World Health Organization's program that was testing them. But no matter how routine an operation is, the patient never seems to be. The checklist made our team discuss each patient's medical and surgical issues before starting. And in the first month, that conversation alone saved a patient's life. We've since caught unrecognized drug allergies, confusion about medications, errors on biopsy specimen labels, and equipment failures. The evidence is: any hospital or surgical staff that operates on patients without a team checklist is endangering them.

What's the most daunting part of being a surgeon?

The complexity. Although there are procedures that we do over and over again, we perform many types of operations only a few times a year. Surgeons need to be able to handle both the routine and the anomalous.

Beyond surgery, medicine as a whole has become extremely complex. Science has enumerated more than 13,000 diagnoses—ways the human body can fail—and found ways to help with nearly all. But these involve more than 6,000 drugs and 4,000 medical and surgical procedures, and those numbers are growing. The volume and complexity of knowledge has exceeded our capacities as individual clinicians.

How can medical professionals cope with such complexity?

You probably think I will say: checklists! But it's deeper than that. What fascinates me about checklists are the values the best ones implicitly contain—humility, discipline, teamwork. Medicine's traditional answer for how professionals should cope with complexity is through training and technology. But we also need the humility to acknowledge that we as individuals will fail at our tasks no matter how smart or experienced we are. We need to believe that discipline in our processes is one way to overcome such failures. And we need to understand that our colleagues, no matter their station or experience, are key assets for helping us maintain vigilance and caring, identify problems, and solve them.

What was the most telling lesson you learned through your research?

Even as they groaned about—or even opposed—having to incorporate the basic checklist into their routine, 93 percent of the surgical staff members we surveyed said they would want *their* surgeons to use it.

What's next on *your* checklist?

It's getting long. By the end of 2010, about 30 percent of U.S. hospitals will have adopted the surgical checklist, and we're working to bring it to the rest and to improve the effectiveness of adoption around the world. The stakes are high: Globally, more than 7 million people a year are left dead or disabled following surgery, about 500,000 in our country alone.

We're now testing crisis checklists for the operating room and, in South India, a WHO Safe Childbirth Checklist. We've also worked with a Boeing safety engineer to design a Checklist for Checklists—which we've posted at projectcheck.org—to help others effectively design their own checklists. And there's much more work to be done. The knowledge exists about what great care requires. It's a matter of putting it into practice.

—Interview by David Cameron

PHOTO: LAURA HANIFIN

CONNECT THE DOCS

THE COMMUNITY OF HMS ALUMNI

President's Report

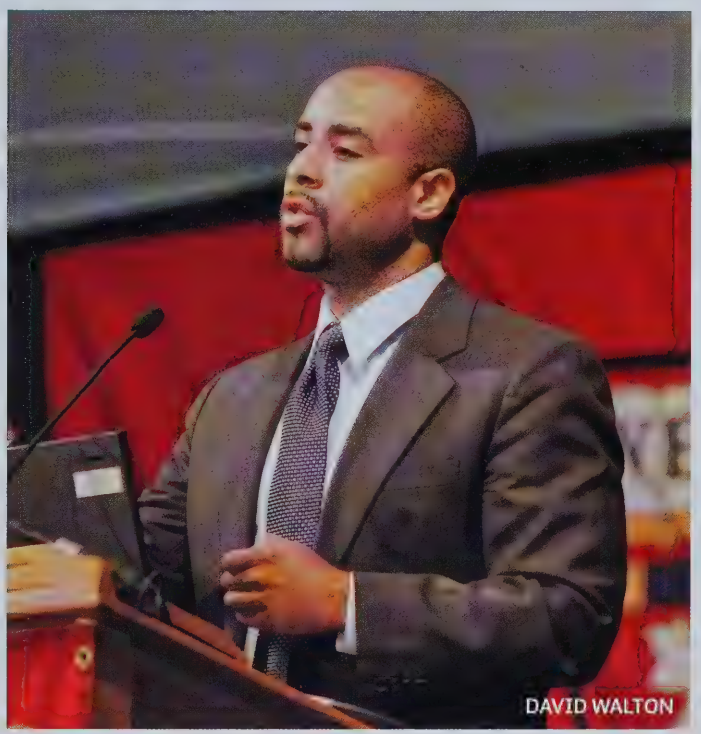
Despite the chill in the air, your Alumni Council members are thinking of spring: what themes should we choose for the Alumni Week symposia on May 26 and 27? Preliminary suggestions include primary care, diversity in medicine, stem cell research, and personalized medicine. We welcome your ideas.

Each year we marvel at the talent we can draw on from our community of alumni. No corner of medicine seems untouched, in fact, by HMS graduates.

Please enjoy your alumni magazine, and send us your thoughts, concerns, and inspirations.

Gilbert Omenn '65 is a professor of internal medicine, human genetics, public health, and bioinformatics at the University of Michigan in Ann Arbor. Send your suggestions to A. W. Karchmer '64, chair of alumni relations, at hmsalum@hms.harvard.edu. To learn more about the alumni community, visit alumni.hms.harvard.edu.

PHOTOS, FROM LEFT: COURTESY OF THE UNIVERSITY OF MICHIGAN; JARROD MCCABE



DAVID WALTON

DELIVERING IN HAITI

Alumni Day focused on the aftermath

When David Walton '03 stepped off the plane in Port-au-Prince, Haiti, just two days after the January 12 earthquake, he viewed a world of devastation and death: buildings destroyed, people with crushed and broken limbs, bodies piled outside morgues.

Several months later, Walton, an HMS instructor in medicine at Brigham and Women's Hospital and deputy chief of mission for Partners In Health in Haiti, was one of several panelists to depict that world during Harvard Medicine in Haiti, the Alumni Day symposium held in late May.

"Our work turned into a triage exercise of patients and medical personnel," Walton said. "Haitian doctors and nurses who hadn't perished were digging out their own families, making it hard to gather a sufficient number of medical professionals for the hospitals." Partners In Health stepped in, tapping more than 4,000 employees from its ten hospitals and clinics in the nation's central region. That relief, Walton said, was augmented by good will and resources from HMS.

Among the first to answer the School's call for help was another panelist, George Dyer '02, an HMS instructor in orthopedic surgery at Brigham and Women's. Dyer arrived in Saint-Marc, a port city about 50 miles from the capital, four days after the quake and helped transform its woefully maintained and equipped hospital into a functioning tertiary care unit.

"Surgery was unending," Dyer said, "and in the early days consisted primarily of amputations. Most patients had four-day-old, gangrenous wounds, and amputation was the only way to save their lives." Dyer expressed pride in the care that team members showed all patients despite cramped quarters, lack of rest, and electrical outages that forced surgeons to don headlamps for illumination.

With seven years of service in Haiti under her belt, panelist Louise Ivers provided additional perspective, explaining that Haiti's devastation was exacerbated by the poverty, poor nutrition, low literacy, and low life expectancy that has long placed it near the bottom of the world's human development index. The earthquake, she said, only served to fragment Haiti's infrastructure further, especially its health care system. An HMS assistant professor of medicine at Brigham and Women's and chief of mission for Partners In Health in Haiti, Ivers said the organization will help rebuild the country's medical education system. Acknowledging the help from the School, she added, "The voice of HMS is a large one that needs to continue."

—*Ann Marie Menting*

CLASS NOTES

NEWS FROM ALUMNI

1952

Samuel Katz

received the 2010 American Society for Microbiology Maurice Hilleman/Merck Award in May. Katz, the Wilburt C. Davison Professor Emeritus at Duke University School of Medicine, was honored for 50 years of vaccine research.

1953

Granville Coggs

"My picture appears in the 2010 Aetna African American History Calendar. I recently began a career as an inspirational speaker, talking about how I've arrived, physically and mentally fit, at age 85."

1954

Nanette Wenger

"This has been a spectacular year for me. I received the Lifetime Achievement Award of the Georgia chapter of the American College of Cardiology, as well as the Hardman Cup Award from the Medical Association of Georgia. I was also recognized by the Georgia State Senate for my contributions to the field of medicine."

1956

John Grover

"Philippa and I remain healthy for our age. We are moving to Chula Vista, California, in September to be near our daughter, Amy. I feel great regret over the death of **Bob Goldwyn**, class agent, good friend, and great person."

Josephine Von Hippel

"I'm glad to be healthy and to know others will now be healthier since we voted for health reform. Eugene, Oregon, has been ahead of the game because we have Volunteers in Medicine. I was happy to work there for eight years as a volunteer psychiatrist after my retirement. Our volunteers treated the working poor who would otherwise not have received any health care."

1957

Thomas Adams

"We now live in the Riverwoods, a continuing care retirement community in Exeter, New Hampshire. It's a great place, in a town with a very good hospital, the cultural benefits of Phillips Exeter Academy, and proximity to mountains and the sea. We moved here five years ago with **John ("Scot") Remensnyder** and his wife, Mary. Scot died in October 2006 in a supportive environment. Mary has stayed, and we remain close friends. **George Baker** and his wife, Bunny, recently moved here. I volunteer at the New Outlook Teen Center and at the Krempels Brain Injury Foundation. In June, Mimi and I attended the 50th anniversary celebration for **Sidney Alexander** and his wife, Susan. My primary care doctor is **Karl Singer '67**, who plays the viola and quotes Maimonides on health."

Thomas J. Gill III

"The Sports Medicine Service at Massachusetts General Hospital continues to expand rapidly under the direction of the chief, my son, **Thomas J. Gill IV '90**. I continue on as director of research and an HMS lecturer on orthopaedic surgery. Amazing where a career in pathology can lead!"

William Greenough III

"I traveled to Dhaka, Bangladesh, in June to celebrate the 50th anniversary of the Charles Research Lab/International Center for Diarrhoeal Diseases Research, where oral rehydration therapy and effective oral vaccines were discovered."

1958

Howard Kremen

"Our youngest daughter, Jessica, is a second-year medical student."

Chris Weatherley-White

"I was recently awarded the Lifetime Volunteer Achievement Award by Operation Smile. I have participated in more than 30 missions for the organization, including five overseas trips this year alone. My current role involves mostly teaching younger surgeons some of the cleft lip and palate surgery 'tricks' I've learned."

PHOTOS: JAN REISS

1959

Boyd Burkhardt
"My wife, Judi, has been stricken with Alzheimer's dementia and is now living separately. My experience at HMS has been unmatched by any other in my life, especially because in that era we were not notified of our grades! Still true?"

1960

Mark Perlroth
"After celebrating our 50th class reunion, I finally understand who all those white-haired people were who were crowding the Quad each spring—they were us! My good health persists, and I am now a grandfather of three."

David Segel
"I'm recovering slowly from a bicycle accident last October. The frontal lobe injury to my dominant sphere has made me more introverted, but I hope to soon be back in my old form."

1961

Mayer Davidson
"I'm still working as the director of a diabetes program at a large outpatient clinic in a medically underserved minority community. I'm also teaching and doing clinical research at Charles Drew University in Los Angeles. I received that school's 2009 Outstanding Professor Award, as well as the 2010 Jefferson Award for Community Service (for cofounding the Venice Family Clinic 40 years ago and continuing to help nurture it as the largest free medical clinic in the country). My third book, *Meeting the American Diabetes Association Standards of Care*, was published early this year."

Royce Moser, Jr.
was recently elected president of the Harvard School of Public Health Alumni Association. Moser continues as a professor in the Department of Family and Preventive Medicine at the University of Utah School of Medicine after having served 23 years as flight surgeon in the U.S. Air Force.

1963

Stephen Howard
"I am now practicing psychiatry two to three days a week at the intake prison for the state of Wisconsin. There I see an amazing variety of people and problems—and I get to leave it all behind when I go home! See you all in 2013."

1964

Frank Williams
"I returned to Bhutan (on my 36th ophthalmic medical mission there) in May 2010, accompanied by my wife, Jackie. We taught medicine, performed eye surgery, and brought with us large amounts of donated medical equipment and supplies. Anyone wishing to assist with these missions can do so through the Frank Williams Foundation, a nonprofit, at my address: 1211 Reynolds Avenue, Clearwater, FL 33756."

1966

Scott Nelson
"I am still working part time as a psychiatrist at a remote Navajo Indian health clinic. I see eight of my ten grandchildren—who live here in New Mexico—often."

1967

Thomas Gutheil
"My daughter, Tia, was accepted into Columbia University Graduate School in creative writing. My son, Dylan, is studying exercise science at Springfield College. My grandson Jake (one of four) earned a yellow belt in tae kwon do."

1968

Thomas Pollard
has been appointed dean of the Graduate School of Arts and Sciences at Yale University, where he is the Sterling Professor of Molecular, Cellular and Developmental Biology.

1970

Richard Stein
"I am course director of Vanderbilt's Introduction to Clinical Problem Solving course at the end of the second year. It's a very rewarding activity but I feel like the world's oldest 'chief resident.'"

1971

N. Emmanuel Cassimatis
"After 34 years with the federal government, in 2009 I moved to Philadelphia to become president of the Educational Commission for Foreign Medical Graduates. My wife, Pat, joined me in January, when she retired from her job at Walter Reed. We love Philadelphia and are always happy to see classmates."

1972

Daniel Doyle
"I continue full-time work as a family and geriatrics physician at the New River Clinic, a community health center in southern West Virginia. This is my 32nd year here. I plan to retire in 2011."

Diane Kittredge
"I was deeply saddened by the death last April of my dear friend and pediatric colleague **Suzanne Riggs**. In the months prior to her

death from pancreatic cancer, she received many honors for her years of work with adolescents, both nationally and in Rhode Island. I know she would have been pleased to see her classmates gathered at her funeral. She always spoke highly of her HMS experience and the scholarship that enabled her to attend."

1973

Donald Weaver
"I continue to enjoy my work at Health Resources and Services Administration helping to improve the health of underserved communities and vulnerable populations. Both of our daughters are married, and Jane and I are the proud grandparents of three-year-old William and one-year-old Ella. If your travels bring you DC way, we'd love to hear from you."

Steven Weinberger
has been named executive vice president and chief executive officer of the American College of Physicians. Weinberger had served as the organization's deputy executive vice president since 2009 and as senior vice president for medical education and publishing since 2004. He is a former president of the Harvard Medical Alumni Association.

1974

Christopher Baker
"Two and a half years later, I still find my position as chair of surgery at Louisiana State University to be a stimulating challenge and New Orleans to be a wonderful city."

1975

David Bor
received the 2010 Art of Healing Award in May from Cambridge Health Alliance, where he is chief of medicine. He is also the Charles S. Davidson Associate Professor of Medicine at HMS.

Mark Shields
"I'm having fun doing clinical integration with 3,500 doctors. Is that even possible? Yes, it is! Nikki and I are in downtown Chicago and loving it. Come visit."

1976

Aloysius Davis
"I am medical director of the Behavioral Health Network, Inc., in Springfield, Massachusetts. I also have a private practice in Longmeadow, Massachusetts. In my spare time, I enjoy fishing, playing chess, and writing."

Deborah German
has been appointed vice president for medical affairs at the University of Central Florida. She will continue her position as founding dean of the university's College of Medicine, which recently welcomed its second class of medical students.

1979

Jill Stein
launched a second run for governor of Massachusetts as a representative of the Green–Rainbow political coalition this past summer.

1980

Ann Errichetti
received the 2010 Healthcare Leadership Award from the Chicago Health Executive's Forum in February. She is the president of Advocate Condell Medical Center in Libertyville, Illinois.

1981

Douglas Peebles
"Still knocking them out and waking them up (most of them, anyway) out here in Framingham, Massachusetts."

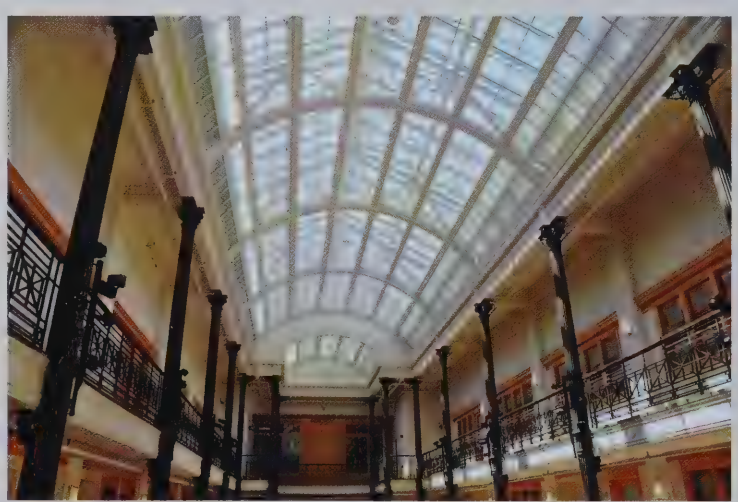


PHOTO: JAN REISS

1982

Charlie Hartness
"My wife, Nancy, and I are enjoying life in Athens, Georgia, where we play string-band music with our friends."

1984

Joan Miller
received the 2010 Joseph B. Martin Dean's Leadership Award for the Advancement of Women Faculty. She is the Henry Willard Williams Professor of Ophthalmology at HMS and chair of the Department of Ophthalmology at the Massachusetts Eye and Ear Infirmary and Massachusetts General Hospital.

1993

Lawrence Bluth
and Heidi Wainman-Bluth have announced the birth of a son, Eli Cameron, on May 16, 2010. He joins Natasha, Samantha, Madison, and Ronan. Bluth, a partner of Hartford Neurology, LLC, in Hartford, Connecticut, was recently appointed associate clinical professor at the University of Connecticut School of Medicine's Department of Neurology.

1996

Elisabeth Hagen
has been confirmed as the undersecretary for food safety at the U.S. Department of Agriculture, where she serves as chief medical officer.

1936

Karl Thomas Langacher

Died May 6, 2010, at the age of 99, in Mansfield, Ohio. Langacher served with the U.S. Army as a captain and chief surgeon in Burma and India before opening a private practice in Mansfield. He also performed general surgery at Mansfield General Hospital for more than 40 years. Langacher was predeceased by his first wife, Helen, in 1987 and by his second wife, Mary Ellen, in 2008. He is survived by his daughters, Mary Robertson and Carol Crouch; six grandchildren; and eight great-grandchildren.

Paul C. Zamecnik

Died October 27, 2009, at the age of 96, in Boston, Massachusetts. Zamecnik helped discover how proteins are made, creating the first cell-free system for studying protein synthesis and identifying transfer RNA. In 1956, he was part of a team that discovered a critical element of the protein synthesis pathway: the ribosome, a cellular component that assembles proteins from amino acids.Two decades later he pioneered antisense technology, a method of attacking harmful viruses and bacteria by blocking the expression of specific genes. Zamecnik joined the HMS faculty as an instructor in medicine at Massachusetts General Hospital, where he remained until retiring as the Collis P. Huntington Professor of Oncologic Medicine, emeritus, in 1979. He was predeceased by his wife of 69 years, Mary Connor, in 2005. Zamecnik is survived by his two daughters, Karen Pierson and Elizabeth Coakley; his son, John; seven grandchildren; and two great-grandchildren.

1938

W. Philip Giddings

Died October 23, 2009, at the age of 96, in Shelburne, Vermont. Giddings served as a captain in the U.S. Army Medical Corps during World War II and received the Purple Heart and the Bronze Star for his participation in the Anzio, Italy, landings. In 1950, he opened a surgical practice in Bennington, Vermont. There he also served as chief of surgery at the Putnam Memorial Hospital from 1950 until 1975. Giddings is survived by his wife of 68 years, Betty; his three sons, Robert, David, and James; a daughter, Deborah; five grandchildren; and five great-grandchildren.

Robert M. Smith

Died November 25, 2009, at the age of 96, in Winchester, Massachusetts. Generally recognized as the father of pediatric anesthesiology, Smith founded the pediatric anesthesia fellowship program at Children's Hospital Boston. He first joined the HMS community as an assistant in anesthesia and served on the staff of Children's, where he was appointed the hospital's first anesthesiologist-in-chief. Smith remained at that hospital for more than three decades, rising to the position of HMS clinical professor of anesthesia. After retiring as clinical professor emeritus of anesthesia in 1980, he practiced at the Franciscan Hospital for Children in Massachusetts from 1980 to 1992. He is survived by two daughters, Marcia and Karen; a son, Jonathan; eight grandchildren; and two great-grandchildren.

William H. Walker

Died December 1, 2009, at the age of 99. Walker spent four years during World War II at the U.S. Army Air Force Regional Hospital in San Antonio, Texas, where he worked as a medical doctor researching pneumonia and infectious mononucleosis. In 1947, he returned to his hometown of Eskridge, Kansas, to take over his father's medical practice, which he ran for 40 years. During that time, Walker was also on the staffs of Stormont Vail and St. Francis hospitals in Topeka, Kansas. He was co-founder of Flint Hills Manor, a skilled nursing facility in the area, and served as its first president and medical director. Walker is survived by his wife of 68 years, Evelyn; his three sons, William, Michael, and Brian; a daughter, Carol; nine grandchildren; and four great-grandchildren.

1942

Robert W. Gage

Died December 19, 2009, at the age of 92, in Amherst, Massachusetts. Gage was a ship's surgeon in the U.S. Navy during World War II. He later worked for eight years as a country doctor in Ulysses, Pennsylvania. In 1960, Gage was recruited to direct and overhaul health services for the University of Massachusetts. One of his most public duties during his eleven years at the school was as team doctor for the UMass basketball and football teams; he treated basketball star Julius Erving, among others. After receiving a master's degree in public health from the Harvard School of Public Health, he returned to UMass as graduate studies director of its public health school. Gage is survived by his wife of 66 years, Peg; his four children, Meg, Jon, David, and Rob; and eleven grandchildren.

1943A

Sidney B. Luria

Died February 27, 2010, at the age of 93, in Highland Beach, Florida. Luria was a medical officer captain in the U.S. Army's 24th infantry in the Pacific theatre during World War II and received a Silver Star, Bronze Star, and Purple Heart for his service. He was later chief of surgery at the Veterans Hospital in Manchester, New Hampshire, before returning to his hometown of Waterbury, Connecticut, to open a private practice. Luria is survived by his wife, Irene.

1943B

Rowland Barnes French

Died July 31, 2009, at the age of 89, in Eastport, Maine. French was assistant director of the tumor clinic at the University of Wisconsin before moving to Eastport in 1953. He remained there as a physician for 37 years, delivering babies and making house calls. French also served as the tuberculosis consultant for Washington County, Maine, and helped to establish the Eastport Health Care Center, which is now named in his honor. French was predeceased by his wife, Winifred, in 1995. He is survived by his four sons, Robert, John, Hugh, and Edward; his daughter, Ann; and three grandchildren.

OBITUARIES

REMEMBERING DISTINGUISHED LIVES

1945

H. Walter Jones

Died on July 28, 2009, at the age of 88, in Boston, Massachusetts, after complications from surgery. Jones served as a captain in the U.S. Army during World War II. He worked as an internist and diabetologist at Massachusetts General Hospital before becoming assistant director of the MIT Medical Department. Jones is survived by his wife, Berys; five sons, Hank, Witmer, David, Ben, and Dan; four stepchildren; twelve grandchildren; and seven step-grandchildren.

1946

Mahlon Hoagland

Died on September 25, 2009, at the age of 87, in Thetford, Vermont. Hoagland served for seven years as assistant professor in what was then the HMS Department of Bacteriology and Immunology. Along with Paul Zamecnik '36, he discovered the initial steps in protein synthesis, amino acid activation, and later transfer RNA. In 1967, Hoagland left HMS to chair the microbiology department at Dartmouth Medical School in Hanover, New Hampshire. After three years at Dartmouth, he moved back to Massachusetts to head the Worcester Foundation. Hoagland retired in 1985. In his later years, he wrote two books, *The Way Life Works*, an introduction to cell biology, and *Exploring the Way Life Works*, a biology textbook. Hoagland was predeceased by a daughter, Susan, in 1973 and by his second wife, Olley, in 2009. He is survived by three children, Robin Hoy, Judy Hauk, and Mahlon "Jay"; five stepchildren; four grandchildren; and two great-grandchildren.

1949

Chester Herrod

Died August 18, 2009, in Napa, California, from complications of Parkinson's disease. Herrod began a private surgical practice in 1960 and was chief of staff at Presbyterian Medical Center from 1965 to 1967. In 1970, he moved to Napa, California, and practiced surgery at Queen of the Valley Hospital there, becoming chief of staff in 1983. He retired in 1987. Herrod is survived by his wife, Ski; his daughters, Kim and Kate; and two grandchildren.

Roger Hickler

Died March 1, 2010, at the age of 84, at his home in Lunenberg, Massachusetts. Hickler served during the Korean War as a naval medical officer at a veterans' hospital in Palo Alto, California. In 1960 he was named a senior associate in medicine and director of what was then Peter Bent Brigham Hospital's Hypertension Laboratory. Hickler left those positions in 1969 to become chief of medicine at Framingham Union Hospital and to join the faculty of Boston University School of Medicine. Two years later, he was recruited to serve as chairman of the Department of Medicine at the newly founded University of Massachusetts Medical School in Worcester. In 1977, he was named director of the Division of Geriatric Medicine and the Lamar Soutter Distinguished Professor of Medicine at that school, positions he held until his retirement in the early 1990s. Hickler was predeceased by his second wife, Dorothy, in 2009. He is survived by two daughters, Sarah and Luisa Geisler; two sons, Matthew and Samuel; three stepsons; and two grandchildren.

William Reagan Owen

Died May 29, 2010, at the age of 84, at his home in Houston, Texas. Owen ran a private cardiology practice for 40 years in Houston. He also served on the teaching staff of the University of Texas, Houston, and as a clinical and associate professor at Baylor College of Medicine. Owen is survived by his wife of 60 years, Margaret; his daughters, Claudia Lummis and Susan Dawson; and five grandchildren.

1952

Joseph A. Rinaldo, Jr.

Died January 29, 2010, at the age of 84, in San Diego, California, after a long struggle with Parkinson's disease. Beginning in 1955, Rinaldo specialized in gastroenterology, first at Henry Ford Hospital and Mt. Carmel Mercy Hospital and later at Providence Hospital, where he served as medical director from 1970 to 1990. He was a founding member and president of the Southeast Michigan Center for Medical Education, an organization that worked toward the establishment of the recently inaugurated Oakland University William Beaumont School of Medicine. Rinaldo later founded the Gastrointestinal Motility Laboratory at the University of California, San Diego School of Medicine. He is survived by his wife of 60 years, Rosemarie; four children, Patrice Cassedy, Barbara Jean, Paul, and Joseph; and five grandchildren.

1953

William R. Collins

Died November 16, 2009, at the age of 83, in Port Ludlow, Washington, after a long illness. Collins practiced as a pediatrician in greater New Bedford, Massachusetts, for 32 years before closing his practice in 1988. He was later named medical director for the Child Protective Services Team in Hawaii and was an associate professor of pediatrics at the University of Hawaii. He retired in 1991. Collins is survived by his wife, Bobbie; two daughters, Nancy Hahn and Kathy Gagliardi; three sons, James, Bruce, and John; and 11 grandchildren.

Norman Weiner

Died March 5, 2009, at the age of 80, in Denver, Colorado. Weiner was an assistant professor of pharmacology at HMS from 1961 to 1967. He then became chairman of the Department of Pharmacology at the University of Colorado Health Sciences Center. Weiner was later appointed Divisional Vice President for Pharmaceutical Discovery at Abbott Laboratories in Chicago, Illinois, but returned to the University of Colorado in 1987, where he remained until his death. Weiner is survived by his wife of 54 years, Diana; five sons, Steven, David, Jeffrey, Gareth, and Eric; and nine grandchildren.

1954

Billy Don Viele

Died August 1, 2009, at the age of 79, in San Diego, California, the

result of a pedestrian accident. Viele was a captain in the U.S. Navy Medical Corps for more than 24 years. In 1978, he opened a gynecology practice in Poway, California, after retiring from the Navy. Viele also served as the medical staff president of Pomerado Hospital in Poway. He is survived by his wife of 59 years, Fran; three sons, Steve, Bob, and Jim; a daughter, Janet; three grandchildren; and one great-grandchild.

1956

Malcolm Brochin

Died November 6, 2009, at the age of 78, in Woodbridge, Connecticut. Brochin was a longtime obstetrician and gynecologist in the New Haven area. He also served as an associate clinical professor of obstetrics and gynecology at Yale University. Brochin was predeceased by a daughter, Martha. He is survived by his wife of 53 years, Betsy; a daughter, Lisa Rosner; a son, Peter; and seven grandchildren.

1962

Edward D. Harris, Jr.

Died May 21, 2010, at the age of 73, in Thetford Hill, Vermont, after a long bout with adenoid cystic carcinoma. Harris was chief of the connective tissue disease section at Dartmouth Medical School and professor and chair of the Department of Medicine at Rutgers Medical School before becoming chair of the Department of Medicine at Stanford University School of Medicine, a position he held from 1987 to 1995. Harris's work at that school significantly advanced the understanding and treatment of rheumatoid arthritis. He remained active in the Stanford community after his retirement, serving as academic secretary from 2002 to 2007 and as professor emeritus until his death. Harris is survived by his longtime companion, Eileen Moynihan; his former wife, Mary Ann Hayward; his sons, Ned, Tom, and Chandler; and four grandchildren.

1966

Robert Trelstad

Died February 15, 2010, at the age of 69, at his home in Princeton, New Jersey, of frontotemporal dementia. Trelstad was an assistant professor of medicine at HMS in 1972. From 1975 to 1981 he was chief of pathology at the Shriners Burn Institute in Boston. He later became the chair of pathology at Robert Wood Johnson Medical School in Piscataway, New Jersey, and in 1998 founded that state's Child Health Institute. Trelstad also created Keyboard Publishing, a company that developed computer-based learning products. He is survived by his wife of 48 years, Barbara; four sons, Derek, Graham, Brian, and Jeremy; and five grandchildren.

1967

Richard A. Garibaldi

Died on September 3, 2009, in West Hartford, Connecticut, of colon cancer. Garibaldi was the E.C. Walker/PHS Professor of Medicine at the University of Connecticut Health Center, chairman of the Department of Medicine at the University of Connecticut, hospital epidemiologist, and special advisor to the State Department of Public Health. He held leadership roles at the American Society of Internal Medicine and the American College of Physicians. He is survived by his wife of 46 years, Lorraine; his daughters, Karen, Christine, and Susanne; his son, Richard; and nine grandchildren.

1981

Ralph L. Warren

Died December 2, 2009, at the age of 55, in Gallup, New Mexico, after a long illness. Warren joined the Massachusetts Air National Guard as a flight surgeon and later served with the New Mexico Air National Guard; he received two Distinguished Service Medals for his service in Iraq. From 1989 through 2000, he practiced general surgery at Massachusetts General Hospital, where he was chief of the surgical intensive care unit. In 2000, Warren left to work with the Indian Health Service at Gallup Indian Medical Center for nine years. Warren is survived by his daughters, Maxine and Madison.

PHOTO: COURTESY OF THE *JOURNAL OF PLASTIC AND RECONSTRUCTIVE SURGERY*

Robert Goldwyn 1930–2010

Robert Goldwyn '56, a witty and cherished member of the Editorial Board of this magazine for more than 40 years, died March 23, 2010, at his home in Brookline, Massachusetts, after a 16-year battle with prostate cancer. He was 79. In 1960, Goldwyn took a two-month leave from his medical training to work with Nobel Laureate Albert Schweitzer in West Africa. Goldwyn later ran a private practice in Brookline for 40 years and was the chief of plastic surgery from 1972 to 1996 at what was then Beth Israel Hospital. He founded the National Archives of Plastic Surgery at HMS in 1972 and was editor of the *Journal of Plastic and Reconstructive Surgery* for 25 years. Throughout his life, he traveled to countries such as Israel and Pakistan to care for victims of war and suicide bombings. He published a collection of essays (*Retired, Not Dead*) in 2009. Goldwyn was predeceased by his first wife, Roberta, in 1994. He is survived by his second wife, Tatyana; three children, Linda, Laura Goodgame, and Peter Robson; and six grandchildren.

Taking a History | Anne Becker

CLAIM TO FAME: Vice Chair, Department of Global Health and Social Medicine, Harvard Medical School

BRIDGING ISLANDS: Thirty years ago, before global health was a Harvard institute—before it was even widely recognized as an academic discipline—it was a passion for the then-teenaged Anne Becker '90. That passion led her to Harvard—first as an undergraduate, then as a student in the inaugural cohort of the Medical School's MD–PhD program in social sciences; then to fieldwork in Fiji, where she began unraveling the complex forces driving eating disorders and suicide risk in adolescents; and then back to HMS, where she is now a professor training future global health leaders.

A HEALTHY APPETITE: On the South Pacific island nation of Fiji, Becker lived in the household of a village chief during her doctoral field research. "When I wasn't working at the local hospital, I was scraping coconuts or fishing," she says. She was fascinated by Fijians' relationship to their bodies—more frank and communal, less self-conscious than those of Americans. And bigger was often better. "People would say, 'You look great! You've gained weight.'"

TUNING IN: In 1995, when television arrived in Fiji, Becker set out to see whether the traditional valuation of robust bodies would protect Fijian girls from the adverse impact of media on body image and the increased risk for eating disorders seen elsewhere. "Unfortunately," she says, "the results were just the opposite." Signs of eating pathology emerged in apparent lockstep with television, as teenage Fijian girls encountered a novel world that seemed to connect thinness with material wealth and autonomy. Becker's follow-up research explored a tangle of generational conflict, domestic violence, youthful hope, and hopeless poverty. Ultimately, she says, "What began as a study about eating pathology became a study about suicide."

SAFETY NET: Poor and politically unstable, Fiji struggles to meet its citizens' mental health needs. Becker has collaborated with Fijian officials to develop a range of strategies, including a pilot program aimed at training teachers to identify and counsel girls at risk for eating disorders and suicide. She plans to return to Fiji in 2012 to evaluate outcomes of this program.

PEER EFFECT: Any solution is complicated, however, by Becker's latest findings, which suggest that a peer network's exposure to television plays a far greater role in Fijian girls' risk for eating pathology than individual viewing habits. "In other words, it doesn't matter whether you watch TV," Becker says. "It matters whether your friends watch TV."

—R. Alan Leo

PHOTO: ROSE LINCOLN/HARVARD NEWS OFFICE

Paul Farmer, MD, PhD, Chair of the Department of Global Health and Social Medicine at Harvard Medical School, is world-renowned for his work building vital health care delivery systems in Haiti and around the globe.

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